

IMPROVING THE MANAGEMENT OF ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Submitted in fulfilment of the requirements for the degree of Doctorate of Philosophy

UNIVERSITY OF TASMANIA



September 2011

DECLARATION OF ORIGINALITY

This thesis contains no material that has been accepted for a degree or diploma by the University or any tertiary institution, except by way of background information and duly acknowledged in the thesis.

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STATEMENT OF ETHICAL CONDUCT

The research associated with this thesis abides by the international and Australian codes on human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University.

Bonnie Bereznicki

STATEMENT OF CONTRIBUTION

The first project, ‘sustainability and feasibility of a community pharmacy intervention to improve the management of asthma’ was designed and conceptualised by Bonnie Bereznicki, Gregory Peterson and Shane Jackson. Bonnie Bereznicki wrote the letters to pharmacists, patients and general practitioners. Peter Gee wrote the data-mining software. Bonnie Bereznicki and Ian DeBoos wrote the qualitative discussion guide. Ian DeBoos and Philippa Hintz performed the participant interviews and qualitative analyses.

The second project, ‘uptake and effectiveness of a community pharmacy intervention to improve the management of asthma’ was designed and conceptualised by Bonnie Bereznicki, Gregory Peterson and Shane Jackson. Bonnie Bereznicki wrote the letters to pharmacists, patients and general practitioners. Peter Gee wrote the data-mining software. Bonnie Bereznicki wrote the software instructions.

The third project, ‘understanding medication persistence in patients with COPD’ was designed and conceptualised by Bonnie Bereznicki, Gregory Peterson, Shane Jackson, David Marshall, Guy Gavagna and Felicity Hardley. Bonnie Bereznicki wrote the letters to pharmacists and patients. Peter Gee wrote the data-mining software. Felicity Hardley and Trish Shee wrote the qualitative discussion guide. Felicity Hardley, Trish Shee, and Randall James performed the participant interviews and qualitative analyses.

Bonnie Bereznicki

ACKNOWLEDGMENTS

I would like to thank the many people who have provided their support, encouragement and guidance throughout my candidature. In particular, Professor Gregory Peterson, Dr Shane Jackson and Professor Haydn Walters have provided the necessary leadership and stimulation to facilitate the successful completion of this body of work.

I would also like to acknowledge the contribution of research colleagues that have provided their assistance with this work. I would like to thank Peter Gee for his dedication to the information technology development required for each project and his patience with the required modifications to the software programs as the projects progressed. I would also like to thank Kimbra Fitzmaurice for her research management skills, and her thoughtful and sensible advice throughout the course of my candidature.

I would like to acknowledge Ian DeBoos and Philippa Hintz for their assistance with the qualitative component of the follow-up asthma study. Thanks also Corinne LeReun for her assistance with the statistical interpretation of the quantitative results.

I would like to offer thanks to Dr Johnson George, Associate Professor Kay Stewart, Tabish Zaidi and Jaya Soma from Monash University; and Dr Geoff March, Mike Quaass and Nicola Hughes from the University of South Australia, who provided their assistance in the planning and implementation stages of the multicentre asthma intervention project. Thanks also to respiratory physicians Dr James Markos, Professor John Wilson and Associate Professor Hubertus Jersmann for their assistance with the pharmacist education sessions.

I would like to acknowledge Dr Guy Gavagna and David Marshall from Boehringer Ingelheim for their assistance in the planning and implementation of the respiratory medication persistence study. Thanks also to Dr Felicity Hardley, Trish Shee and Randall James from P Group Research for their assistance with the qualitative component of this study.

I would also like to thank Cathy Beswick and Glenn Freeman from the Tasmanian Asthma Foundation, and Garry Irving from the Asthma Foundations Australia for their continuous support and advice over the course of my candidature. Thanks also to members of the Tasmanian Asthma Foundation Medical and Scientific Advisory Committee for their enthusiasm and interest towards my work.

I would like to acknowledge the support of a number of funding bodies that provided support for this body of work. The Asthma Foundations Australia not only funded my Honours project, but also financially supported the follow-up asthma study described in this thesis, via an Asthma Targeted Intervention Grant. The multicentre asthma intervention project was funded by the Australian Government Department of Health and Ageing through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia, and the respiratory medication persistence study was funded by Boehringer Ingelheim Australia. I am confident that these funding bodies have invested in the future of asthma and COPD management in Australia. I would also like to thank the participating community pharmacists, general practitioners and patients for their cooperation and support throughout each of the projects.

I am grateful for the support of my colleagues at the Tasmanian School of Pharmacy and the Unit for Medication Outcomes Research and Education, for their support and encouragement. I would also like to acknowledge the School in providing the resources and facilities required throughout the course of my candidature. I look forward to continuing my research within the School.

Lastly, I would like to thank my family and friends who have provided me with the support necessary to continue this work to completion. I am grateful to my parents for their unconditional love and support, and for teaching me that anything is possible. In particular I would like to thank my wonderful husband Luke for his understanding, patience, advice and unwavering support over the past three years. I would also like to thank my gorgeous baby boy Ryan for his beautiful, patient temperament that allowed me to write up my thesis from home over the last year.

PUBLICATIONS

All publications listed here resulted from work described in this thesis.

Peer-reviewed publications

Bereznicki BJ, Peterson GM, Jackson SL, *et al.* The sustainability of a community pharmacy intervention to improve the quality use of asthma medication. *J Clin Pharm Ther* 2011; 36: 144-151.

Bereznicki BJ, Peterson GM, Jackson SL, *et al.* Perceived feasibility of a community pharmacy-based asthma intervention: a qualitative follow-up study. *J Clin Pharm Ther* 2011; 36: 348-355.

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Bereznicki BJ, Peterson GM, Jackson SL, *et al.* Pharmacist-initiated general practitioner referral of patients with suboptimal asthma management. *Pharm World Sci.* 2008; 30: 869-875.

Conference abstracts

Bereznicki B, Peterson G, Jackson S, *et al.* A community pharmacy intervention program to improve the quality use of asthma medication: uptake and effectiveness. *National Medicines Symposium*. Melbourne 2010 [oral presentation].

Bereznicki B, Peterson G, Jackson S, *et al.* Understanding medication persistence in patients with COPD. *National Medicines Symposium*. Melbourne 2010 [oral presentation].

Bereznicki B, Peterson G, Jackson S, *et al.* The sustainability of a community pharmacy intervention to improve the quality use of asthma medication. *National Medicines Symposium*. Melbourne 2010 [poster].

Bereznicki B, Peterson G, Jackson S, *et al.* Perceived feasibility of a community pharmacy-based asthma intervention: a qualitative follow-up study. *National Medicines Symposium*. Melbourne 2010 [poster].

Bereznicki B, Peterson G, Jackson S, *et al.* A community pharmacy intervention program to improve the quality use of asthma medication: participant satisfaction. *National Medicines Symposium*. Melbourne 2010 [poster].

Bereznicki B, Peterson G, Jackson S, *et al.* A community pharmacy intervention program to improve the quality use of asthma medication. *Pharmacy Practice Research Summit*. Canberra 2010 [oral presentation].

Bereznicki B, Peterson G, Jackson S, *et al.* A community pharmacy intervention program to improve the quality use of asthma medication: uptake and effectiveness. *Pharmacy Practice Research Summit*. Canberra 2010 [poster].

Bereznicki B, Peterson G, Jackson S, *et al.* A community pharmacy intervention program to improve the quality use of asthma medication: participant satisfaction. *Pharmacy Practice Research Summit*. Canberra 2010 [poster].

Bereznicki B, Peterson G, Jackson S, *et al.* The sustainability of a community pharmacy intervention to improve the management of asthma. *Australasian Pharmaceutical Society Association Conference*. Hobart 2009 [oral presentation].

Bereznicki B, Peterson G, Jackson S, *et al.* Perceived feasibility of a community pharmacist-led asthma intervention: a qualitative follow-up study. *Australasian Pharmaceutical Society Association Conference*. Hobart 2009 [poster].

Bereznicki B, Jackson S, Peterson G, *et al.* Drivers and barriers of tiotropium persistence in patients with COPD. *Thoracic Society of Australia and New Zealand Annual Scientific Meeting*. Darwin 2009 [poster].

Bereznicki B, Jackson S, Peterson G, *et al.* Understanding medication persistence in patients with COPD. *Australasian Pharmaceutical Society Association Conference*. Canberra 2008 [oral presentation].

Bereznicki B, Peterson G, Jackson S, *et al.* The use of pharmacy medication records to prompt GP referral of patients with suboptimal asthma management. *Australian Asthma Conference*. Sydney 2008 [oral presentation].

Bereznicki B, Peterson G, Jackson S, *et al.* A community pharmacy-based intervention to improve the quality use of asthma medication. *National Medicines Symposium*. Canberra 2008 [oral presentation].

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ABBREVIATIONS

AAP	Asthma Action Plan
BMQ	Beliefs About Medicines Questionnaire
BOLD	Burden of Obstructive Lung Disease [study]
CI	Confidence interval
COMPASS	COMPArison of Symbicort® and Seretide® [study]
COPD	Chronic obstructive pulmonary disease
DALY	Disability adjusted life year
ED	Emergency department
FDA	Food and Drug Administration
FEV1	Forced expiratory volume in one second
FVC	Forced vital capacity
GAPP	Global Asthma Physician Patient [study]
GINA	Global Initiative for Asthma
GOAL	Gaining Optimal Asthma controL [study]
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GP	General practitioner
HADS	Hospital Anxiety and Depression Scale
HEPA	High-efficiency particulate air
HFA	Hydrofluoroalkane
HMR	Home medication review
ICAS	International Control of Asthma Symptoms [study]
ICS	Inhaled corticosteroid(s)
ICU	Intensive care unit
Ig	Immunoglobulin
INSPIRE [study]	Investigating New Standards for Prophylaxis in Reducing Exacerbations [study]
IPQ	Illness Perception Questionnaire
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
LABA	Long-acting beta-2 agonist
LTRA	Leukotriene receptor antagonist
MiniAQLQ	Mini Asthma Quality of Life Questionnaire

N/A	Not available
NAC	National Asthma Council
NNH	Number needed to harm
NNT	Number needed to treat
NRT	Nicotine replacement therapy
OR	Odds ratio
OTC	Over-the-counter
PACP	Pharmacy Action Care Program
PaO ₂	Partial pressure of oxygen in the blood
PEF	Peak expiratory flow
PhARIA	Pharmacy Access / Remoteness Index of Australia
P : R	Preventer-to-reliever
QOL	Quality of life
RCT	Randomised controlled trial
RM	Respiratory medication
RR	Relative risk
SABA	Short-acting beta-2 agonist
SD	Standard deviation
SGRQ	St. George's Respiratory Questionnaire
SMART	Symbicort® Maintenance And Reliever Therapy
TABS	Tool for Adherence Behaviour Screening
TORCH	TOward a Revolution in COPD Health [study]
UK	United Kingdom
US	United States

ABSTRACT

Asthma and chronic obstructive pulmonary disease (COPD) are among the top ten most common chronic diseases in Australia,¹ causing significant social and economic burden on the patient, family and healthcare system. More than five million Australians are affected by asthma or COPD, and each year these diseases disrupt daily life and productivity of many individuals and contribute to thousands of deaths.² Despite the availability of safe and effective respiratory medication, problems such as under-diagnosis, medication adherence issues and poor understanding of asthma and COPD, have led to the conditions being poorly managed in Australia.^{3,4} The work described in this thesis was directed at learning more about how asthma and COPD are managed in the community and steps that can be take to improve the management of these conditions.

Community pharmacists assisted in the implementation of all of the projects described in this thesis. Community pharmacists are ideally placed in the healthcare system to help patients manage chronic diseases in view of their expertise, their regular contact with patients and their accessibility. Community pharmacists also have access to patients' dispensing records, meaning they are uniquely placed to monitor medication adherence issues. The projects described in this thesis utilised an innovative software application ('MedeMine') to data mine pharmacy dispensing records and target patients with asthma or COPD, as evidenced by the supply of specific medications.

Part One of this thesis describes two projects targeted at patients with poorly managed asthma. The first project was a follow-up study of a previous intervention conducted in Tasmanian community pharmacies that saw patients with potentially poorly managed asthma referred to their general practitioner (GP) for an asthma management review. The intervention resulted in a three-fold improvement in the management of asthma, as measured by the ratio of dispensed preventer to reliever medications.⁵ A follow-up of the intervention was conducted to determine whether the improvement in asthma management was sustained, and qualitative interviews were conducted with patients, community pharmacists and GPs, to determine the perceived feasibility of the intervention. The project showed significant, sustained improvements in the ratio of dispensed preventer medications to reliever medications for at least 12 months after the intervention. The qualitative component of this project indicated that a wider roll-out of

the asthma intervention, with an improved process for involving GPs, would be feasible and well accepted. Further research should determine the best approach in influencing patients' perceptions of asthma control and whether these perceptions are amenable to a more intensive educational intervention. This could result in more efficient asthma interventions, translating to improved patient outcomes.

The second project was designed to test the uptake and effectiveness of two different types of community pharmacy-based asthma intervention across three Australian states. Community pharmacies throughout South Australia, Tasmania and Victoria participated. The project utilised MedeMine to identify patients whose asthma may not be well managed, as evidenced by a high provision of reliever medications. The uptake and effectiveness of mailed and face-to-face pharmacist interventions were studied. Significantly fewer face-to-face interventions were offered to patients compared with mailed interventions, and lack of time was the main reason cited for not offering face-to-face interventions. There were significant improvements in the ratio of dispensed preventer medication to reliever medication after each intervention, but these improvements were limited by pharmacists' uptake of the face-to-face intervention. Time constraints in busy pharmacies may restrict the uptake and effectiveness of face-to-face interventions in the 'real world' setting, making mailed interventions an attractive option. Pharmacists should have both mailed and face-to-face intervention options available to ensure maximum uptake and effectiveness of the interventions.

Part Two of this thesis describes a study that aimed to understand the drivers and barriers of persistence with respiratory medication, specifically tiotropium, in patients with COPD. MedeMine was installed in pharmacies throughout Tasmania, Australia, and patients who were likely to be persistent or non-persistent with tiotropium were identified. Patients completed questionnaires and qualitative interviews. Patients' perceptions of the risks and benefits of tiotropium, which appeared to be strongly influenced by personal experience and the prescriber's attitude, were found to be determinants of persistence. Identification of these variables can facilitate the development of interventions that modify or take account of specific patient adherence behaviours and perceptions about the risks and benefits of medication. It is evident that increased awareness of the patients' beliefs about medicines is needed among healthcare providers, and patients should be encouraged to express their views about medicine in order to optimise and personalise their therapy.

This body of work presents a number of solutions to issues surrounding the management of asthma and COPD in the community. With the knowledge gained from the results of these projects and using aspects of interventions described in this thesis, community pharmacists can dramatically improve the management of these conditions. Community pharmacists have the necessary skills to communicate with other healthcare providers and patients themselves to improve the management of asthma and COPD, and software tools such as MedeMine can aid in the efficient targeting of high-risk patients. A national roll-out of the asthma intervention, and a specifically designed COPD intervention, would result in better health outcomes for patients, and ultimately less burden on the health system.

PART ONE:

INTRODUCTION AND OBJECTIVES

Asthma and chronic obstructive pulmonary disease (COPD) are among the top ten most common chronic diseases in Australia,¹ causing significant social and economic burden on the patient, family and healthcare system. More than five million Australians are affected by asthma or COPD, and each year these diseases disrupt daily life and productivity of many individuals and contribute to thousands of deaths.² Despite the availability of safe and effective respiratory medication, problems such as under-diagnosis, medication adherence issues and poor understanding of asthma and COPD, have led to the conditions being poorly managed in Australia.^{3,4}

Despite its national health priority status, the management of asthma remains a problem in Australia. Research has shown that a significant proportion of people with asthma still do not have a written AAP, have poorly controlled asthma and over-rely on their reliever medication.⁶ Patients need to be more educated about asthma and the need for regular preventive therapy and monitoring, so that their perceptions of asthma control are more realistic. Healthcare professionals should also work together to encourage patients to be more forthcoming about their asthma symptoms, so that their therapy can be tailored and optimised to ensure adequate asthma control.

There is irrefutable evidence that COPD is a significant public health problem in Australia. Unlike asthma, however, it is not a National Health Priority area, despite a mortality rate ten times that of asthma and annual costs that exceed \$8 billion.^{7,8} This suggests a lack of awareness of the present and future burden from COPD, perceptions and societal stigmas around its cause, and insufficient understanding of its public health importance.⁹ In order to reduce the burden of COPD in Australia, it is imperative that healthcare professionals develop a collaborative management approach to ensure the early and accurate diagnosis of COPD, which can then drive the implementation of effective treatments. Patients should also be encouraged to express their views about the condition and its treatment in order to optimise and personalise their therapy, ensuring adherence and persistence with prescribed medications.

Pharmacists are ideally placed in the healthcare system to address asthma and COPD management issues and they have the necessary skills to communicate with other

healthcare providers and patients themselves to improve these conditions. There is enormous scope for community pharmacists to become the feedback link between patients and GPs, which would answer the societal need for improved management of asthma and COPD. Community pharmacists are trained in counselling and educating patients about their condition and prescribed medications, and have access to patients' dispensing records, meaning they are uniquely placed to monitor medication adherence issues.

Community pharmacists assisted in the implementation of all of the projects described in this thesis. While there clearly is the potential for community pharmacists to have an impact in improving the management of asthma and COPD, such approaches are most likely to be successful if they can be easily integrated into pharmacists' workflow, and the need for further research testing strategies that are pragmatic in busy community pharmacies has been identified.¹⁰⁻¹⁴

The work described in this thesis was directed at learning more about how asthma and COPD are managed in the community and steps that can be take to improve the management of these conditions. The aims of each project descried in this these were to:

- Determine the sustainability and perceived feasibility of a multidisciplinary intervention that utilised community pharmacy dispensing records to identify and educate patients with suboptimal asthma management;
- Utilise community pharmacy dispensing records to test the uptake and effectiveness of two different types of community pharmacy-based asthma interventions across three Australian states; and
- Understand the reasons why patients with COPD do and do not persist with prescribed medication.

With the knowledge gained from the results of these projects and using aspects of interventions described in this thesis, it is hoped that community pharmacists will gain more potential to dramatically improve the management of these conditions.

PART TWO:

IMPROVING THE MANAGEMENT OF ASTHMA

CHAPTER ONE: INTRODUCTION

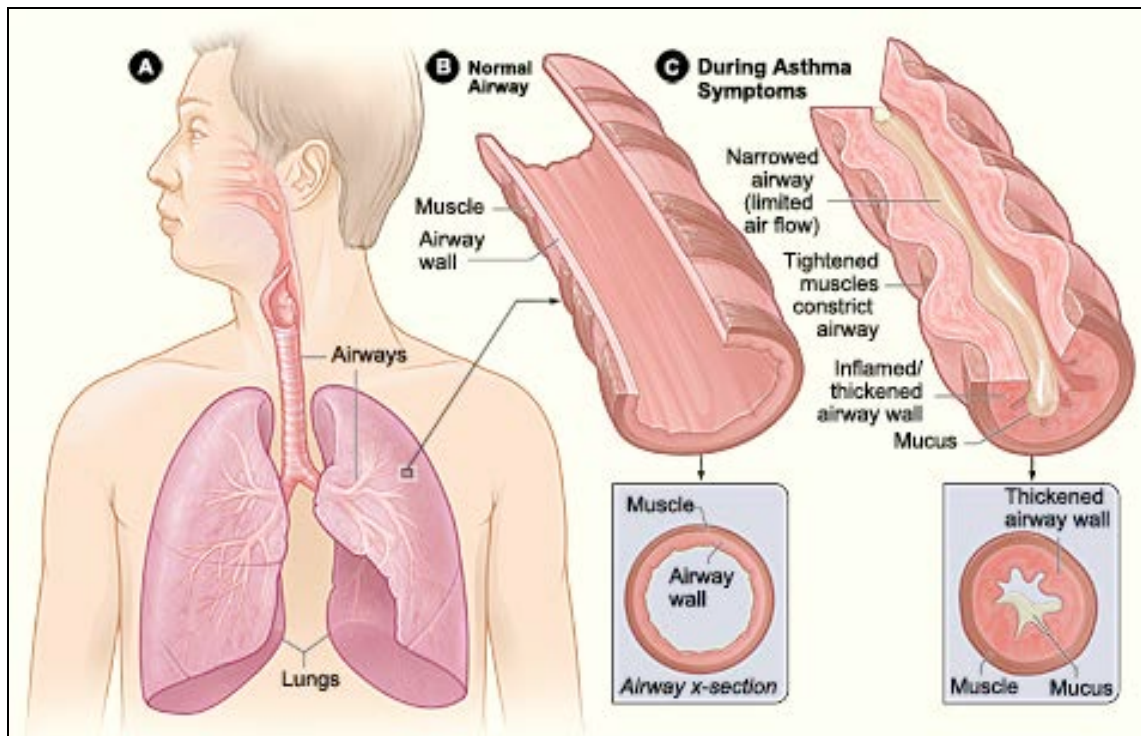
1.1 Pathophysiology of asthma

Asthma is a disorder defined by its clinical, physiological and pathological characteristics. The predominant feature is episodes of shortness of breath and wheezing. In fact, the word ‘asthma’ comes from the Greek word ααζειν (aazein), which translates as ‘to breathe with open mouth or to pant.’¹⁵ Currently, the Global Initiative for Asthma (GINA) definition is:

“Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or early in the morning. These episodes are usually associated with widespread, but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment.”¹⁶

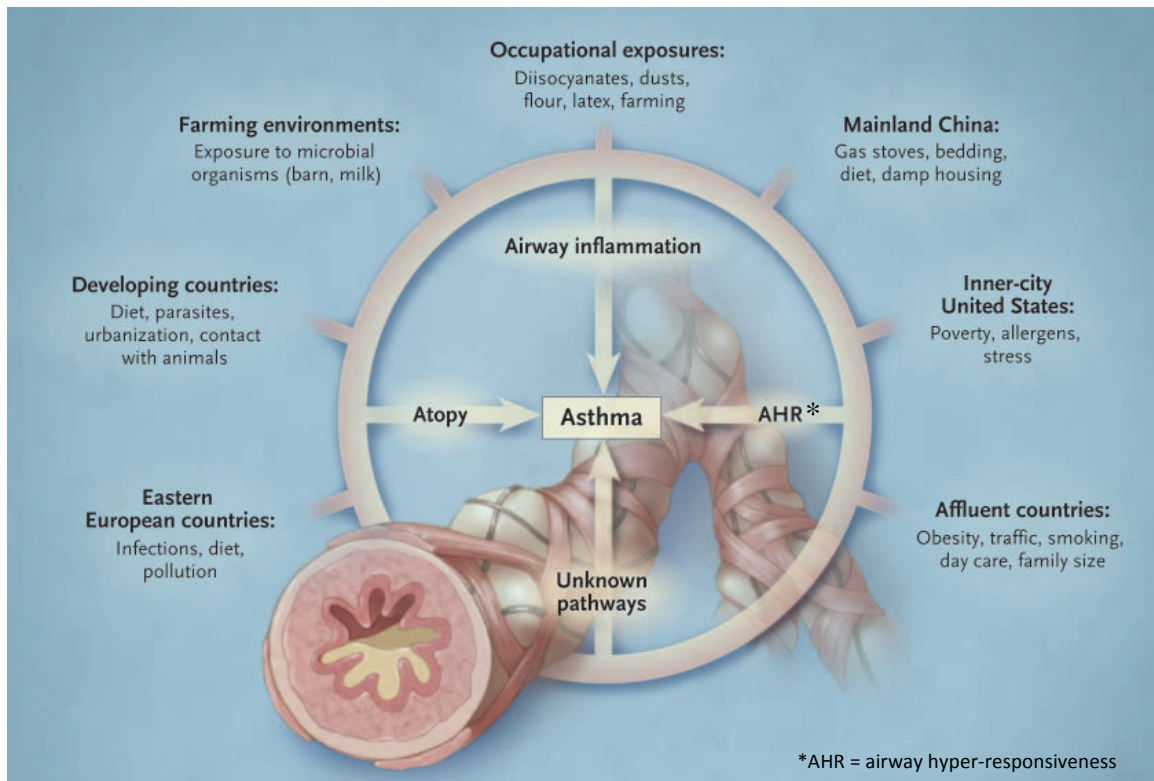
The symptoms of asthma are due to bronchoconstriction, excess mucus production and airway inflammation (Figure 1). Episodes of worsening symptoms, or asthma exacerbations, are an exaggerated lower airway response to an environmental exposure, such as respiratory virus infections, allergens, pollutants, medications or other irritants.¹⁷ Structural changes reported in the airways of patients with asthma include epithelial fragility, goblet cell hyperplasia, enlarged submucosal mucus glands, angiogenesis, increased matrix deposition in the airway wall, increased airway smooth muscle mass, wall thickening and abnormalities in elastin.¹⁸ These alterations are thought to be due to genetic influences, early life exposures, duration of disease and long-term uncontrolled inflammation.¹⁸

Figure 1. Illustrative representation of the pathophysiological changes in asthma¹⁹



For many patients, asthma begins in infancy, and both genetic and environmental factors contribute to its inception and evolution.²⁰ The mechanisms whereby these factors influence the development of asthma are complex, and it is likely that key genes interact both with environmental factors and with other genes to determine asthma susceptibility.^{21,22} The apparent racial and ethnic differences in the prevalence of asthma reflect underlying genetic variances with a significant overlay of socioeconomic and environmental factors (Figure 2).²³

Figure 2. Effect of the interaction of various types of exposures and genetic backgrounds on the prevalence of asthma²³



In western medicine, use of bronchodilators for the treatment of asthma started at the beginning of the twentieth century,²⁴ and it was not until the 1960s that airway inflammation was recognised as an underlying feature.^{25,26} With the recognition that immunologically-mediated responses are integrally linked to the development of airway inflammation and hence the inception, persistence and severity of disease, treatment of asthma is now being directed principally toward these factors.²⁰ This led to the rationale of corticosteroids, now the mainstay of asthma therapy.¹⁶ There is now good evidence that the clinical manifestations of asthma can be controlled with appropriate treatment.²⁷ When asthma is controlled, there should be no more than the occasional recurrence of symptoms and severe exacerbations should be rare.¹⁶

1.2 Burden of asthma

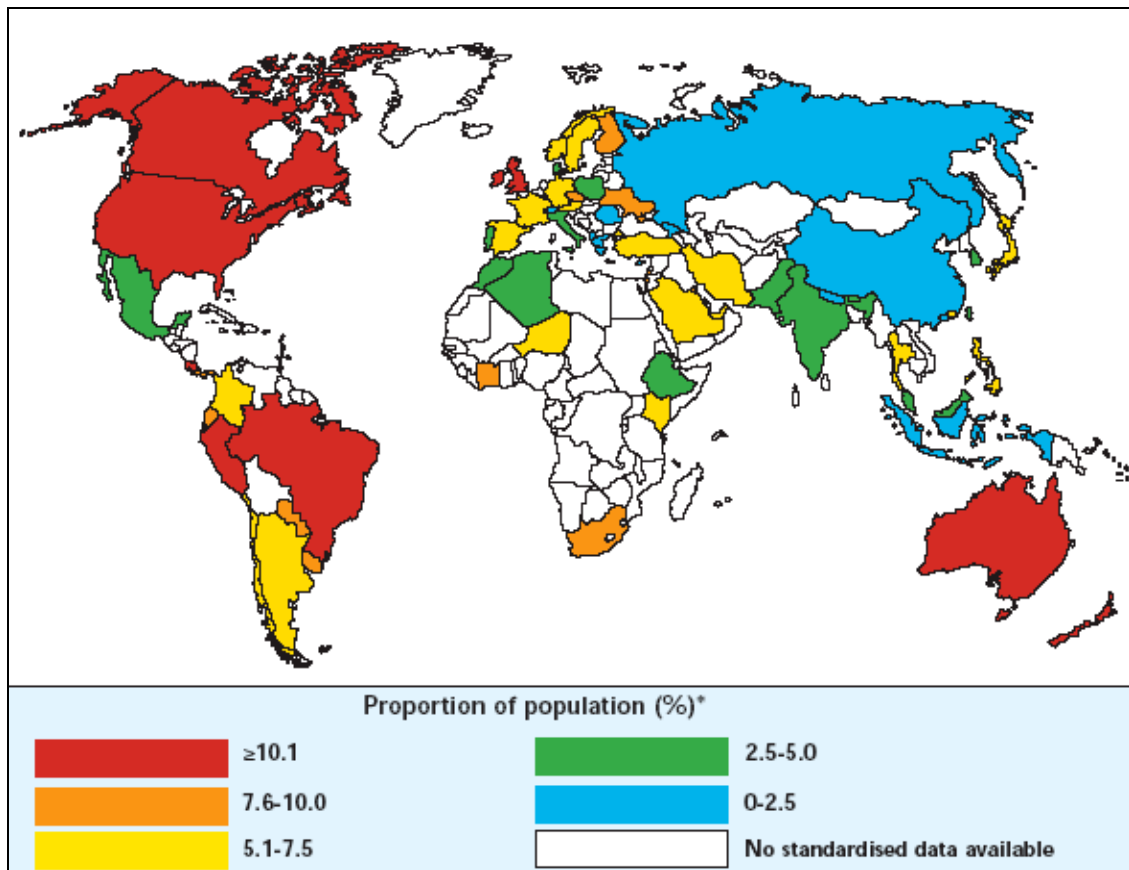
Asthma is a significant health issue worldwide and is the focus of various clinical and public health interventions. It is one of the most common chronic diseases in the world, affecting an estimated 300 million people.²⁸ The prevalence of asthma increases as communities adopt western lifestyles and become urbanised, and the prevalence is expected to increase to 400 million by 2025.²⁸ Both morbidity and mortality from

asthma are high despite treatment that is effective for the majority of patients. Even in developed countries where patients have easy access to treatment, asthma is often under-recognised and under-treated, and sometimes fatal.

The number of disability-adjusted life years (DALYs) lost due to asthma worldwide is estimated to be 15 million per year, which is similar to that for diabetes, liver cirrhosis and schizophrenia.²⁹ It is estimated that asthma accounts for one in every 250 deaths worldwide.²⁸ Many of these deaths are preventable and are due to suboptimal long-term medical care and delay in obtaining help during the final attack.

International population-based studies suggest that Australia has one of the highest prevalence rates for asthma in the world,³⁰ affecting an estimated two million people, or 10-12% of the Australian population (Figure 3).^{6,8,31} Exacerbations of asthma lead to approximately 40,000 hospitalisations and 105,000 emergency department (ED) visits annually.⁶ In 2003, asthma was the eleventh-leading contributor to the overall burden of disease in Australia, accounting for 2.4% of the total number of DALYs.³² In the 2000-01 financial year, health expenditure due to asthma was \$693 million, which was 1.4% of the total health expenditure in that year.³³ In 2006, asthma was identified as the underlying cause of 402 deaths (139 males and 263 females).⁸

Figure 3. World map of the prevalence of clinical asthma³⁰



Poorly controlled asthma has been shown to have significant detrimental effects on quality of life, performance of daily activities,³⁴⁻³⁷ and has been associated with depression.^{38,39} Patients with uncontrolled asthma have significantly more exacerbations, leading to urgent GP visits, ED visits and hospitalisations, and consequently higher treatment costs than those with controlled asthma.⁴⁰⁻⁴²

Asthma has a measurable impact on how people assess their overall health status. The 2004-05 National Health Survey showed that among people with asthma, 42% rated their health as 'excellent' or 'very good,' compared to 58% of people without asthma. On the other end of the scale, 28% of people with asthma rated their health as 'poor' compared to only 14% of people without asthma.³¹ Most of the impact of asthma is on physical functioning and on the ability to perform social roles, such as work or study.

It is also known that asthma significantly affects quality of life (QOL) and psychological health. A South Australian study reported a higher prevalence of depression among people with asthma compared with people without asthma.⁴³ Furthermore, it was found that people with more severe symptoms of asthma (shortness

of breath, waking at night with asthma symptoms or morning symptoms) were more likely to suffer from major depression than those without severe symptoms. Quality of life scores were also lower for the same groups.

Findings from the 2004-05 Australian National Health Survey showed that the burden of asthma in Australia declined and that some improvements in asthma management occurred between 2001 and 2004-05.³¹ However, despite the existence of governmental⁴⁴ and non-governmental⁴⁴ initiatives aiming to improve asthma care, the results also suggested that socioeconomic disparities are widening and there are still a number of areas for improvement. Significant clinical problems persist, including under-diagnosis,^{3,45} limited asthma knowledge,³ under-treatment with inhaled corticosteroids (ICS),^{3,31,46} limited possession of written Asthma Action Plans (AAPs)^{3,31,46-49} and poor patient management skills.⁵⁰ This evidence suggests that there needs to be further research into the most effective way to educate people about asthma, maintain their knowledge and empower them to take responsibility for managing their asthma effectively.³

1.3 Asthma control

The assessment of asthma control has become pivotal in the management of asthma. However, several surveys in developed nations have shown that the majority of patients with asthma do not enjoy adequate asthma control.^{31,51-56}

Asthma control refers to control of the clinical manifestations of the disease, and is the ultimate goal of asthma management.¹⁶ There is a clear relationship between asthma severity and asthma control. The underlying severity of asthma in a patient may be modified by changes in the environment and by the treatment received for asthma. Ultimately, the changes in these environmental and treatment factors will impact on the patient's symptoms and their ability to function. Asthma control reflects the combined effect of underlying disease severity, environmental exposures and the effectiveness of treatment.⁵⁷

A number of patient-related variables may influence asthma control. Laforest *et al.* identified several independent patient-related determinants of inadequate asthma control, including female gender, active smoking and overweight status.⁵⁸ Control also varied according to the type of asthma supervision. Patients supervised exclusively by

specialists (rather than GPs) were more likely to have their asthma properly controlled. Patients who were dispensed combined long-acting beta-2 agonist (LABA) and ICS therapy were also more likely to have their symptoms properly controlled, particularly at higher doses.

The Australian National Asthma Council (NAC) recommends the day-to-day management of asthma, including adjustment of medications, should closely depend on ongoing assessment of asthma control.⁵⁹ Current asthma guidelines suggest a series of criteria to assess if asthma is controlled, as displayed in Table 1.

Table 1. Assessment of asthma control⁵⁹

Parameters	Level of asthma control		
	Good	Fair	Poor
Daytime symptoms	None	< 3 days per week	≥ 3 days per week
Night-time symptoms	Not woken	≤ 1 night per week	> 1 night per week
Physical activity	Normal	Normal	Restricted
Exacerbations	None	Mild, infrequent	Moderate-severe, frequent
Missed work/school	None	None	Any
Reliever use*	None	< 3 doses per week	≥ 3 doses per week
Lung function (PEF and FEV ₁) [†]	Normal	≥ 90% personal best	< 90% personal best

*Does not include one dose per day for prevention of exercise-induced symptoms. [†]PEF = peak expiratory flow; FEV₁ = forced expiratory volume in one second.

Asthma control tools are a useful aid in measuring a patient's asthma status and are designed to support patient consultations.⁵⁹ The Asthma Control Test is a patient-based tool developed⁶⁰ and validated⁶¹ for identifying patients with poorly controlled asthma. The five-item test is designed to measure the patient's level of asthma control during the preceding four weeks. Items relate to activity limitation, shortness of breath, nighttime symptoms, use of short-acting beta-2 agonists (SABAs) and a self-assessment of asthma control. The overall score (the 'Asthma Score') out of 25 is given by the addition of the response to each item, with a score of 20-25 classed as 'on target' and a score of 19 or less as 'off target' (Figure 4). It has been demonstrated that the asthma score has a good predictive ability against outcomes related to asthma and also a good ability to detect risk factors.⁶² The responsiveness of the Asthma Control Test to changes in asthma control and lung function has also been reported.⁶¹

Figure 4. The Asthma Score⁶³

The Asthma Score questionnaire consists of five questions (Q1 to Q5) with five possible answers each, ranging from 1 to 5. The questions are as follows:

- Q 1** In the **past 4 weeks**, how often did your asthma prevent you from getting as much done at work, school or home?
 1 All of the time, 2 Most of the time, 3 Some of the time, 4 A little of the time, 5 Not at all.
- Q 2** During the **past 4 weeks**, how often have you had shortness of breath?
 1 More than once a day, 2 Once a day, 3 3 to 6 times a week, 4 Once or twice a week, 5 Not at all.
- Q 3** During the **past 4 weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
 1 4 or more times a week, 2 2 to 3 nights a week, 3 1 night a week, 4 Less than 1 night a week, 5 Not at all.
- Q 4** During the **past 4 weeks**, how often have you used your reliever medication (such as Ventolin®, Asmol®, Airomir®, Epaq®, Bricanyl®)?
 1 3 or more times a day, 2 1 or 2 times per day, 3 2 or 3 times per week, 4 Once a week or less, 5 Not at all.
- Q 5** How would you rate your asthma control during the **past 4 weeks**?
 1 Not controlled, 2 Poorly controlled, 3 Somewhat controlled, 4 Well controlled, 5 Completely controlled.

To the right of the questions is a large circle labeled "SCORE" for the final result.

GlaxoSmithKline Australia has created a website whereby a patient’s Asthma Score can be easily calculated, using validated questions regarding asthma control.⁶³ Healthcare professionals can log in to the site and there is a link available to print out a copy of the Asthma Control Test for patients to complete, with a referral form to the patient’s GP to use if necessary. The Asthma Foundations and the NAC, as well as the Pharmacy Guild and Pharmaceutical Society of Australia, support the Asthma Score. The Asthma Score is a helpful screening tool to distinguish patients with good symptom control from patients with poor symptom control in an objective and feasible way.⁶⁴ In particular, the Asthma Score can help health professionals identify patients with uncontrolled asthma and facilitate their ability to follow the patient’s progress with treatment.

Achievement of asthma control is the aim of asthma management. To achieve this goal it is imperative that asthma be treated and monitored appropriately. GINA stated the following in regards to the achievement of asthma control:

“Complete control of asthma is commonly achieved with treatment, the aim of which should be to achieve and maintain

control for prolonged periods, with due regard to the safety of treatment, potential for adverse effects, and the cost of treatment required to achieve this goal.”¹⁶

The individual goals of successful asthma management, as outlined in the GINA guidelines, are shown in Table 2.¹⁶ The development of international¹⁶ and national⁵⁹ guidelines for the management of asthma attempts to help the achievement of these goals become a reality.

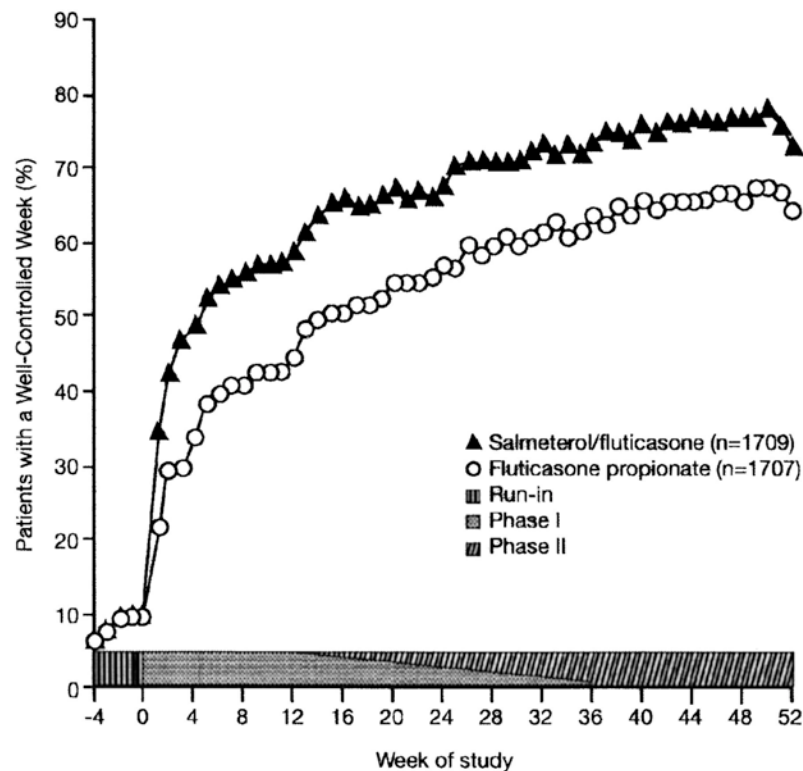
Table 2. Goals of asthma management¹⁶

1. Achieve and maintain control of symptoms
2. Maintain normal activity levels, including exercise
3. Maintain pulmonary function as close to normal as possible
4. Prevent asthma exacerbations
5. Avoid adverse effects from asthma medications
6. Prevent asthma mortality

These goals reflect the understanding of asthma as a chronic inflammatory condition that requires ongoing monitoring and management. The first goal, “to achieve and maintain control of symptoms,” implies that controlling symptoms by suppressing and reversing inflammation is more desirable than treating symptoms as they arise.

The international Gaining Optimal Asthma control (GOAL) study sought to investigate if guideline-defined asthma control was achievable in 3,421 patients with uncontrolled asthma.²⁷ This study found that in the majority of patients with uncontrolled asthma across a wide range of severities, control of asthma (measured by PEF, rescue medication use, symptoms, night-time awakenings, exacerbations and adverse effects of medication) could be achieved and maintained (Figure 5). Furthermore, in stepping up treatment in attempt to achieve guideline-defined total control, even those patients who did not attain the authors’ stringent definition of control showed considerable improvements in health status and a reduction in exacerbation rates.

Figure 5. Patients achieving a well controlled week in the GOAL study²⁷



Phase I: Dose escalation phase: treatment stepped up until total control achieved, to a maximum of 500 µg of ICS daily. Phase II: Patients remained on the dose reached in phase I.

The GOAL study clearly demonstrated that optimal asthma control can be achieved and should be the aim of treatment. The approach of aiming for total control and maintaining treatment resulted in the virtual elimination of exacerbations and near-normal QOL in the majority of patients.²⁷ The findings were strengthened by the large size of the study, which involved subjects over a wide range of age, geographic location, ethnicity and baseline treatment. Subsequently, international¹⁶ and national⁵⁹ treatment guidelines refer to this study as evidence that the goals of asthma management can be achieved and maintained with appropriate preventive therapy.

1.4 Guidelines for the management of asthma

While the drug treatments used in the management of asthma have proven efficacy, effective management strategies are imperative to ensure their appropriate use and reduce morbidity and mortality of the disease. To achieve and maintain asthma control for prolonged periods, recommendations for asthma management have been laid out in a number of interrelated components. These components include:

- Development of a patient/healthcare professional partnership;

- Identifying and reducing exposure to risk factors, monitoring control through assessment of symptoms and medication use; and
- Establishing individual plans for disease management and for managing exacerbations.^{16,65}

Several barriers have been shown to reduce the availability, affordability, dissemination and efficacy of optimal asthma therapies. As well as the patient barriers identified (such as poor education, culture differences and low income), the lack of symptom-based guidelines and low public health priority have been recognised as barriers to reducing the burden of asthma.^{28,29} In 1989, the GINA program was initiated in an effort to raise awareness among public health and government officials, healthcare professionals and the general public that morbidity due to asthma was on the increase.²⁸ GINA works with health professionals around the world in an attempt to reduce asthma prevalence, morbidity and mortality through resources such as evidence-based guidelines for asthma management. The management of asthma has improved considerably over the past decade; the World Health Organisation states “asthma management plans have reduced mortality and severity in countries where they have been applied.”²⁹

In Australia, the NAC was launched in 1989, with the major objective of improving asthma management in Australia through an educational strategy and the implementation of an Australian Asthma Management Plan.⁶⁶ The NAC was an initiative of the stakeholders in asthma care (Thoracic Society of Australia and New Zealand, Royal Australian College of General Practitioners, Pharmaceutical Society of Australia and the Asthma Foundations Australia) with support from the pharmaceutical industry to promote common approaches to asthma management.⁶⁶ The Australian Asthma Management Plan provided guidance and recommendations for health professionals in the management of asthma according to a Six Step Plan (Table 3).

Table 3. The Australian Six Step Asthma Management Plan⁵⁹

1. Assess asthma severity
Assess overall severity when the patient is stable, not during an acute attack
2. Achieve best lung function
Treat with intensive asthma therapy until 'best' lung function is achieved
Back-titrate to lowest dose that maintains good symptom control and best lung function
3. Maintain best lung function: identify and avoid trigger factors
Identify and avoid trigger factors and inappropriate medication
4. Maintain best lung function: optimise medication program
Treat with the least number of medications and use the minimum doses necessary
Ensure the patient understands the difference between 'preventer,' 'reliever,' and 'symptom controller' medications
Take active steps to reduce the risk of adverse effects from medication
5. Develop an action plan
Discuss and write down an individualised care plan for the management of exacerbations
Detail the increase in medication doses and include when and how to gain rapid access to medical care
6. Educate and review regularly
Ensure patients and their families understand the disease, the rationale for their treatment and how to implement their action plan
Review inhaler technique at each consultation
Review adherence at each consultation

After the implementation of these consensus-based guidelines, there was evidence to suggest that the NAC may have contributed to increased awareness and improved management of asthma in Australia.⁶⁷ However, during the late 1990s it became clear that a higher level of activity was needed to maintain the progress of the NAC, as asthma management was still suboptimal.^{49,50,68}

In recognition of the significant burden that asthma places on the Australian community in terms of health, social, economic and emotional costs, Australian Health Ministers announced asthma as a National Health Priority Area in 1999.⁶⁹ Subsequently, the Commonwealth Government announced the \$48.4 million National GP Asthma Initiative in the 2001 National Health Budget to improve health outcomes of people with moderate-to-severe asthma. The GP Asthma Initiative promotes the use of the Asthma Cycle of Care (formerly the Asthma 3+ Visit Plan), which utilises a structured approach to asthma care, as the best practice model of managing asthma, recognising that effective long-term management of asthma requires ongoing care and regular review. The Asthma Cycle of Care has largely replaced the Six Step Asthma

Management Plan in general practice. Currently, the two most important resources for asthma management in Australia are the Asthma Cycle of Care and the Asthma Management Handbook.⁷⁰

The Asthma Cycle of Care encourages partnerships in proactive asthma care between the patient and their health professionals, and involves at least two asthma-related consultations within 12 months for a patient with moderate-to-severe asthma. The visits include an assessment of asthma severity and level of asthma control, a review of the patient's use of asthma-related medication and devices, and asthma self-management education. An integral part of the Asthma Cycle of Care is the development of a written Asthma Action Plan (AAP), which helps the patient or carer recognise worsening asthma and adjust asthma therapy accordingly, in an attempt to prevent severe exacerbations.

At a minimum, the Asthma Cycle of Care must include:

- At least two asthma related consultations within 12 months for a patient with moderate-to-severe asthma;
- At least one of these consultations (the review consultation) to have been planned at a previous consultation;
- Documentation of diagnosis and assessment of asthma severity and level of asthma control;
- Review of the patient's use of, and access to, asthma related medication and devices;
- A written asthma action plan (or documented alternative if the patient is unable to use a written action plan);
- Provision of asthma self-management education; and
- Review of the written or documented asthma action plan.^{70,71}

Ongoing patient education is vital to creating a partnership between patients and healthcare professionals, which can then contribute to successful asthma care.⁶⁵ However, it has been shown that the acquisition of knowledge by patients does not necessarily translate into effective self-management behaviour.^{72,73} It is therefore imperative that the patient not only understands their condition, including the purpose of

medication and inhalation technique, but also the importance and value of self-monitoring and self-management of their asthma. Overall, four main components of asthma education programs have been identified:

- Information about asthma;
- Self-monitoring;
- Regular medical review; and
- A written action plan.⁷⁴

The NAC also publishes the Asthma Management Handbook, which is revised every 3-4 years. It comprises guidelines for delivery of best-practice asthma care in general practice plus practical strategies for implementation.⁷⁰

The Asthma Management Handbook aims to help clinicians and other health professionals make changes in their practice based on sound evidence, and where evidence is lacking, the consensus opinion of Australian experts has been incorporated. The Handbook acknowledges the difficulties of providing organised care in the primary care setting and tries to provide practical strategies that will assist with diagnosis, ongoing management and patient education. While primarily aimed at GPs, the Handbook is also intended as a resource and teaching tool for community pharmacists, nurses, asthma educators, ambulance officers, consumer representatives and healthcare students, emphasising a team approach to asthma care. The latest (2006) edition contains:

- Updated diagnostic, management and prescribing guidelines;
- Expanded material on asthma and allergy, exercise-induced asthma, occupational asthma, asthma in pregnancy and in older people and co-morbidities;
- More detail on diet and complementary medicine;
- New chapters on smoking cessation and asthma prevention; and
- Practical advice on providing structured asthma care in the primary care setting.⁵⁹

The Asthma Management Handbook and the Asthma Cycle of Care remain the backbone of asthma care in Australian general practice. However, a number of Australian studies have reported that, unfortunately, asthma management still falls well short of the NAC guidelines. Research has shown that a significant proportion of people

with asthma still do not have a written AAP,^{3,31,46-48} have poorly controlled asthma, and do not regard asthma as a chronic disease, but rather an intermittent problem requiring emergency management.⁷⁵⁻⁷⁷ It is unclear whether incomplete implementation of the NAC guidelines is the result of time shortage or lack of interest on the part of the GP or the patient. There is evidence to suggest that even extensive educational strategies have limited impact on clinical care and outcomes.⁷⁸ There are clearly barriers to the implementation of certain components of the guidelines, particularly in light of the evidence for low rates of AAP possession and use of ICS, which need to be overcome.


1.5 Self-management plans

An integral part of the Asthma Cycle of Care is the development of a written AAP, which helps the patient or carer recognise worsening asthma. AAPs have become a core component of asthma management in Australia in accordance with best practice guidelines. The idea of a written action plan is that the patient is given a set of rules by which to alter therapy, dependent on either PEF monitoring or symptom levels. The implication is that an appropriate, early response to deterioration will prevent dangerous exacerbations and will generally improve health-related QOL. AAPs contain four essential components:

- Instructions on when to increase treatment;
- How to increase treatment;
- The duration of the treatment increase; and
- When to cease self-management and seek medical help.⁷⁹

An individualised AAP should be tailored to the patient's underlying asthma severity and treatment. An example of an AAP template developed by the NAC, the Australian Department of Health and Ageing, and the Asthma Foundations Australia as part of the Asthma Cycle of Care,⁸⁰ is shown in Figure 6.

Figure 6. Asthma Action Plan template⁸⁰

ASTHMA ACTION PLAN										
Name:	Date:	Best Peak Flow* <small>*Not recommended for children under 12 years</small>								
WHEN WELL Asthma under control (<i>almost no symptoms</i>) <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 50%;">Preventer</td> <td style="width: 50%;">Dose</td> </tr> <tr> <td>Reliever</td> <td>Dose</td> </tr> <tr> <td>Symptom controller (if prescribed)</td> <td>Dose</td> </tr> <tr> <td>Combination medication (if prescribed)</td> <td>Dose</td> </tr> </table>		Preventer	Dose	Reliever	Dose	Symptom controller (if prescribed)	Dose	Combination medication (if prescribed)	Dose	Peak flow above <div style="border: 1px solid black; width: 50px; height: 20px; margin: 0 auto;"></div>
Preventer	Dose									
Reliever	Dose									
Symptom controller (if prescribed)	Dose									
Combination medication (if prescribed)	Dose									
WHEN NOT WELL Asthma getting worse (<i>waking from sleep, first sign of a cold, using more reliever</i>) <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 50%;">Preventer</td> <td style="width: 50%;">Dose</td> </tr> <tr> <td>Reliever</td> <td>Dose</td> </tr> </table> Continue symptom controller Continue combination medication Continue on this increased dosage for before returning to the dose you take when well		Preventer	Dose	Reliever	Dose	Peak flow between <div style="border: 1px solid black; width: 50px; height: 20px; margin: 0 auto;"></div> and <div style="border: 1px solid black; width: 50px; height: 20px; margin: 0 auto;"></div>				
Preventer	Dose									
Reliever	Dose									
IF SYMPTOMS GET WORSE Asthma is severe (<i>difficulty with normal activity, feel that asthma is out of control</i>) Start prednisolone/prednisone and contact doctor Dose <ul style="list-style-type: none"> Stay on this dose until your peak flow is above on two consecutive mornings Reduce prednisolone/prednisone to dose daily for days, then cease Extra steps to take: When your symptoms get better, return to the dose you take when well.		Peak flow between <div style="border: 1px solid black; width: 50px; height: 20px; margin: 0 auto;"></div> and <div style="border: 1px solid black; width: 50px; height: 20px; margin: 0 auto;"></div>								
DANGER SIGNS <i>(symptoms get worse very quickly, need reliever more than 2 hourly)</i> Continue reliever <div style="border: 2px solid red; padding: 5px; display: inline-block; margin-top: 10px; color: red; font-weight: bold;">Dial 000 for ambulance</div>		Peak flow below <div style="border: 1px solid black; width: 50px; height: 20px; margin: 0 auto;"></div>								
Doctor's stamp and/or contact details:		Pharmacist's stamp and/or contact details:								
<small>© 2008 National Asthma Council Australia</small>										

A key part of AAP use is helping people with asthma to observe themselves and their own actions, and learn from these to support self-care behaviours and integrate these

into their daily routines.⁷⁹ Increasing patient participation in their own care has been shown to be associated with improved asthma management, independent of asthma symptoms.⁸¹ Gibson *et al.* found that patients with asthma have a strong desire for knowledge of their condition, but do not prefer to make decisions alone during an exacerbation. The preferred option is for joint decision making between the patient and GP.⁸² On the other hand, Adams *et al.* reported that patients preferred GPs to assume the major role in most decision-making about their management. However, they wished to retain control in choosing when to seek care and wanted shared decisions regarding initiating changes in medications during a moderate exacerbation.⁸³ In fact, it has been shown that lower preferences for autonomy in decision making with regard to initiating treatment changes during an asthma exacerbation are associated with an increased risk of admission to hospital with asthma.⁸⁴

It is essential that the provision of a written AAP be coupled with self-management education and regular GP reviews. Together, these are high-profile parts of Steps 5 and 6 of the Australian Asthma Management Plan: ‘develop an action plan’ and ‘educate and review regularly.’ A systematic review of 36 RCTs provided evidence that the use of a written AAP in conjunction with training in self-management and regular medical review improves health outcomes in patients with asthma.⁷⁴ Self-management education reduced hospitalisations (relative risk [RR] 0.64, 95% confidence interval [CI] 0.50-0.82), ED visits (RR 0.82, 95% CI 0.73-0.94), unscheduled visits to the doctor (RR 0.68, 95% CI 0.56-0.81), days off work or school (RR 0.79, 95% CI 0.67-0.93), nocturnal asthma (RR 0.67, 95% CI 0.56-0.79) and QOL (standard mean difference 0.29, 95% CI 0.11-0.47). Furthermore, evidence from a case-control study of people who had died from asthma showed that the presence of a written AAP was associated with a 70% reduction in the risk of death.⁸⁵

1.6 Pharmacological therapy

1.6.1 Short-acting beta-2 agonists

Short-acting beta-2 agonists (SABAs) such as salbutamol and terbutaline are the mainstay drugs for acute relief of asthma symptoms, and the prevention of exercise-induced bronchoconstriction.⁵⁹ Asthma management guidelines recommend that an inhaled SABA be prescribed as standard reliever therapy and should be carried by all

patients with symptomatic asthma (except those using Symbicort[®] Maintenance And Reliever Therapy).^{16,59}

The beta agonists, one of the oldest classes of drugs used in medicine, were used in the treatment of asthma long before their mechanism was understood.⁸⁶ Non-selective adrenoceptor agonists have been used to relieve bronchoconstriction for at least 5,000 years, but were only introduced into western medicine in the 1920s.⁸⁷ More selective beta-2 agonists, such as fenoterol, salbutamol and terbutaline, were developed in the 1960s.²⁴

The link between the use of SABA and the rising asthma death rate has been the subject of ongoing debate.⁸⁸ A number of studies have implicated regular and perhaps excessive use of SABA in asthma deaths and near-death emergencies⁸⁹⁻⁹⁵ and worse clinical outcomes.⁹⁶⁻⁹⁸ While the epidemic deaths from asthma have only occurred with isoprenaline and fenoterol, both of which have subsequently been withdrawn from the market,⁸⁶ salbutamol has never been associated with an increased risk of asthma deaths, despite the very high sales in many countries.⁹⁹ The concerns about adverse outcomes with frequent and regular SABA use are likely to have mainly been related to suboptimal use of ICS in patients whose asthma was inadequately controlled and treated.⁸⁵

The development of tolerance to bronchodilator activity may be a concern with patients' prolonged use of SABAs.¹⁰⁰ Some studies have shown a reduction in bronchodilator response with prolonged treatment with SABAs,¹⁰¹⁻¹⁰³ while others have shown that patients with asthma are resistant to the development of SABA tolerance.¹⁰⁴⁻¹⁰⁶ Multiple mechanisms may modulate clinical responses to SABAs, such as genetic variation, receptor function, coexisting bronchial inflammation and interactions with other drugs.¹⁰⁷ Genetic polymorphisms affecting amino-acids at positions 16 and 27 within the beta-2 receptor gene have been implicated in the asthma phenotypes and influence on the variability observed in response to use of bronchodilator agents used in the treatment of asthma.^{108,109}

A systematic review of 44 RCTs gave reassuring evidence against the concerns over regular use of SABAs.¹¹⁰ All trials consisted of an experimental group (who were given a SABA regularly, together with a SABA for rescue use) and a control group (who were given a matching placebo for regular use with an SABA for rescue use). While the

regular treatment groups required less rescue medication and had fewer days with asthma symptoms, no significant differences were found in airway calibre measurements or exacerbation rates. Nevertheless, SABAs are recommended in all stages of asthma on an as-needed basis only, as they do not treat the underlying inflammation. Increasing use of SABAs is a warning of deterioration of asthma control and indicates the need to reassess management.¹⁶

1.6.2 Inhaled corticosteroids

Current international¹⁶ and Australian⁵⁹ guidelines recommend that all patients with persistent asthma of all levels of severity use ICS as preventive therapy. ICS are currently the most effective anti-inflammatory medications for the treatment of persistent asthma. Their clinical benefits include decreased asthma symptoms,¹¹¹⁻¹¹⁴ improved lung function,¹¹¹⁻¹¹⁴ fewer exacerbations,¹¹⁵ fewer hospitalisations¹¹⁶⁻¹²⁰ and fewer asthma-related deaths.¹²¹⁻¹²⁴ However, they do not cure asthma, and when they are discontinued deterioration of clinical control follows within weeks to months in a proportion of patients.¹²⁵⁻¹²⁷

It is well established that in adults, persistent asthma requires regular long-term preventive medication to maintain good control.¹²⁸ Evidence-based guidelines over the past decade, including the NAC's Six Step Asthma Management Plan, have emphasised the importance of the regular use of anti-inflammatory drugs (preferably ICS) as first-line therapy for anything more severe than occasional mild asthma and a shift of approach away from reliance on relievers. Asthma guidelines recommend that maintenance ICS be prescribed at the lowest effective dose according to the severity of the condition.^{16,59} The NAC recommends that treatment with ICS should be considered for patients with any of the following:

- Exacerbations of asthma in the last two years;
- Use of reliever medication three times a week or more;
- Asthma symptoms three times a week or more;
- Waking at least one night per week due to asthma symptoms; and/or
- Impaired lung function.⁵⁹

There have been a number of studies in the international literature indicating that a high usage of reliever medication, relative to preventer medication, is associated with poorer clinical outcomes of asthma, including increased ED visits and hospital admissions.^{117,129-132} Eisner *et al.* found that dispensing of medium to high level ICS therapy was associated with a reduced risk of intensive care unit (ICU) admission, whereas high level inhaled beta-2 agonist dispensing was associated with an increased risk of both ICU admission and endotracheal intubation for asthma. Importantly, stratified analysis indicated that this excess risk was observed only among patients not receiving ICS therapy.¹³¹ Salamzadeh *et al.* reported similar findings: patients who had a lower ratio of regularly prescribed preventers to relievers were prescribed more oral prednisolone rescue courses for acute exacerbations. The authors mentioned that GPs and/or patients tended to control the asthma worsening episodes by prescribing/taking more relievers rather than preventive anti-inflammatory inhalers which are recommended as the mainstay of treatment.¹²⁹

It has been reported that for patients with asthma who require ICS, starting at a moderate dose (Table 4) is equivalent to starting with a high dose and stepping down, and that initial medium ICS doses appear to be more effective than an initial low ICS dose.¹³³ It is essential that the ICS treatment is individualised, as too high a dose may result in adverse effects and too low a dose may result in under treatment and poor asthma control.

Table 4. ICS daily dose equivalents: what is meant by low, medium and high daily doses?⁵⁹

Dose level	Ciclesonide	Beclomethasone-HFA*	Fluticasone	Budesonide
Low	80-160 µg	100-200 µg	100-200 µg	200-400 µg
Medium	160-320 µg	200-400 µg	200-400 µg	400-800 µg
High	Over 320 µg	Over 400 µg	Over 400 µg	Over 800 µg

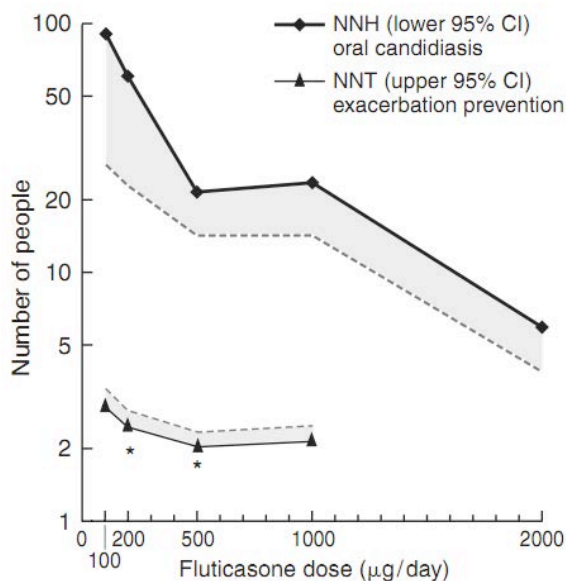
*HFA = Hydrofluoroalkane

While the available ICS differ in their potencies, (beclomethasone-HFA equivalence: beclomethasone-HFA 100 µg = fluticasone 100 µg = budesonide 200 µg = ciclesonide 80 µg¹³⁴⁻¹³⁶) available evidence suggests that they have similar clinical effects at equivalent doses.¹³⁷⁻¹⁴⁰ ICS demonstrate a relatively flat dose-response relationship for the majority of important clinical efficacy measures, however, patients with more severe symptoms and poorer asthma control may benefit from higher doses.¹⁴¹⁻¹⁴³ In mild-to-

moderate asthma, marked clinical improvements have been seen in most studies in the low-to-moderate dose range.¹⁴¹⁻¹⁴³ Doses in excess of that range increase the risk of systemic adverse effects.¹⁴⁴

More pronounced than the dose-related clinical effects of ICS, are the dose-related adverse effects. For most patients, the main effect of increasing ICS dose in asthma is to increase adverse effects, with little additional benefit to the patient (Figure 7).

Figure 7. Comparison of the relative effects of increasing doses of fluticasone in asthma¹⁴⁵



Results for fluticasone are displayed in terms of benefit (number needed to treat; NNT) and harm (number need to harm; NNH) on a logarithmic scale, with the relevant portion of the 95% CI (shaded area).

*Significant heterogeneity present ($P < 0.05$).

There is an increased risk of systemic adverse effects with long-term treatment with high dose ICS. An important adverse effect is dose-related suppression of the hypothalamic-pituitary-adrenal axis. A systematic review of 27 RCTs found that marked adrenal suppression occurs with high doses of ICS above 750 µg per day (fluticasone-equivalent).¹⁴⁶ Other dose-related adverse effects, such as osteoporosis, glaucoma, cataracts and skin thinning are largely restricted to adult patients treated long-term with high dose ICS.

Of particular concern to parents is growth suppression from ICS, and a number of studies have been conducted to determine the effect of ICS on height. In the Prevention of Early Asthma in Kids trial the difference in growth rate was significant between the fluticasone and control groups in the first year of the study (6.6 ± 1.0 cm per year in the

fluticasone group versus 7.3 ± 1.0 cm per year in the placebo group, $P < 0.01$), but not during the second year of treatment.¹⁴⁷ In the third year observation period, the children who had been regularly treated with ICS grew more quickly than the children in the control group (7.0 ± 0.8 cm per year versus 6.4 ± 0.9 cm per year, $P < 0.01$). In the Childhood Asthma Management Program study, children using inhaled budesonide were 1.1 cm shorter than the controls at the end of the four-year treatment phase.¹⁴⁸ However, a 14-year prospective study of children treated with budesonide found that while growth decreased significantly after commencing budesonide, from a mean of 6.1 cm per year (95% CI 5.7-6.5) to 5.1 cm per year in the first year (95% CI 4.7-5.5, $P < 0.001$) and 5.2 cm per year in the second year (95% CI 5.1-5.9, $P < 0.05$), subsequent growth was no different to controls.¹⁴⁹ Furthermore, there was no relation between the initial reduction in growth rate after commencing ICS therapy and the difference between predicted and attained adult height, suggesting that the initial growth suppression was transient and had little long-term consequence. Evaluation of growth in children with asthma is complicated, because the severity of asthma has been demonstrated to have a significant negative correlation with height, regardless of ICS therapy.¹⁵⁰ Although the apparent safety of low dose ICS in children with respect to growth suppression seems evident, it remains important to monitor growth in all children who take ICS long-term, at any dose.⁵⁹

Because of the potential of ICS for causing dose-related adverse effects, asthma management guidelines recommend a reduction in their dose once asthma control is established.^{16,59} In particular, the NAC recommends that the step-down of ICS should be considered after effective asthma control has been in place for 6- 12 weeks, decreasing the dose by approximately 25 to 50% each time.⁵⁹ There is evidence that a reduction in ICS dose can be achieved by adopting a sensible step-down approach, without compromising asthma control.¹⁵¹

1.6.3 Long-acting beta-2 agonists

Long-acting beta-2 agonists (LABAs), or ‘symptom controllers,’ provide prolonged bronchodilation, reduction in day- and night-time symptoms, improved quality of sleep and reduced requirement for SABAs.¹⁵² However, while salmeterol is a partial agonist at the beta-2 receptor, achieving maximum effect after about 60 minutes,¹⁵³ eformoterol is almost a full agonist, achieving a more rapid onset of action with substantial effect at

five minutes similar to salbutamol.¹⁵⁴ In contrast to SABAs, LABAs were designed specifically for regular use, as their duration of action is at least 12 hours. LABAs were introduced as prospective ‘symptom controllers,’ to prevent symptoms, whether spontaneous or due to some environmental or activity-related airway hyper-responsiveness.¹⁵⁵ The results of 31 RCTs have demonstrated that regular use of LABAs gives significantly better asthma control, as measured by lung function and frequency of symptoms, than regular use of SABAs.¹⁵⁶ While a decrease in lung function has been demonstrated with SABAs,^{101,102} no tendency to develop tolerance has been demonstrated with salmeterol^{157,158} or eformoterol.¹⁵⁹⁻¹⁶¹

A systematic review of 67 RCTs (42,333 patients) demonstrated significant advantages of LABA treatment compared to placebo, regardless of whether patients were taking ICS or not.¹⁶² Patients treated with LABAs demonstrated significantly improved lung function, as demonstrated by improved morning PEF, evening PEF and FEV₁, significantly fewer symptoms, less use of rescue medication and higher quality of life scores.

When LABAs were first developed and marketed, concerns about the link between regular use of SABA and asthma deaths were the subject of ongoing debate. It was initially suggested that LABAs could be free of the fatal adverse drug reactions associated with their short-acting counterparts.¹⁶³ Since then, two large RCTs have been performed to test the hypothesis that the use of LABAs in patients with asthma is associated with a increased risk of death.^{164,165}

The Serevent[®] Nationwide Surveillance Study was a 16-week RCT whereby 25,180 patients with asthma were randomly allocated to salmeterol 50 µg twice daily or salbutamol 200 µg four times daily.¹⁶⁴ The only significant difference between the groups was the number of medical withdrawals due to asthma, which were fewer with salmeterol than with salbutamol (2.91% versus 3.79%, $\chi^2 = 13.6$, $P < 0.001$). Death due to any cause occurred in 0.32% of the patients in the salmeterol group and in 0.24% of the patients in the salbutamol group (RR 1.35, $\chi^2 = 1.3$, $P = 0.25$). The corresponding figures for death due to asthma or airway disease were 0.07% and 0.02% (RR 3.00, $P = 0.11$). The main conclusion of this trial was that more deaths occurred with salmeterol but, compared with salbutamol, this difference was not statistically different.

The Salmeterol Multicenter Asthma Research Trial was a 28-week safety study that compared salmeterol 42 µg twice daily to placebo in the treatment of patients with asthma.¹⁶⁵ Following an interim analysis of 26,355 patients, the study was terminated due to an excess of respiratory-related deaths in the salmeterol group. Respiratory-related deaths occurred in 0.18% of the patients in the salmeterol group and in 0.08% of the patients in the placebo group (RR 2.16, 95% CI 1.06-4.41, $P < 0.05$). The corresponding figures for asthma-related deaths were 0.10% and 0.02% (RR 4.37, 95% CI 1.25-15.34, $P < 0.05$), and for combined asthma-related deaths or life-threatening experiences were 0.28% and 0.17% (RR 1.71, 95% CI 1.01-2.89, $P < 0.05$). Post-hoc exploratory subgroups suggested that African-Americans and those not on ICS at baseline were at particular risk of respiratory- or asthma-related deaths or life-threatening experiences.

In a recent systematic review, the data from the two large studies^{164,165} were combined; in patients who were not taking ICS, compared to regular salbutamol or placebo, there was a significant increase in risk of asthma-related death with regular salmeterol (odds ratio [OR] 9.52, 95% CI 1.24-73.09).¹⁶⁶ Because the confidence interval was wide, it could not be concluded that the ICS abolish the risks of regular salmeterol. In addition, the review of 26 RCTs comparing salmeterol to placebo found that all cause mortality was higher with regular salmeterol than placebo, but the increase was not significant (OR 1.33, 95% CI 0.85-2.10). However, non-fatal serious adverse events were significantly increased when regular salmeterol was compared to placebo (OR 1.14, 95% CI 1.01-1.28). Similarly, a systematic review of 22 RCTs comparing eformoterol to placebo found that all cause mortality was higher with regular eformoterol than placebo, but the increase was not significant (OR 1.52, 95% CI 0.24-9.71). Again, non-fatal serious adverse events were significantly increased when regular eformoterol was compared to placebo (OR 1.57, 95% CI 1.05-2.37).¹⁶⁷

While acknowledging the value of LABAs in asthma treatment, asthma management guidelines insist that these drugs should only be used alongside ICS either as separate inhalers or, preferably as combination products in the same inhaler. LABA monotherapy is not recommended.^{16,59}

1.6.4 Combination therapy

The addition of LABA to ICS should be considered when asthma symptoms or suboptimal lung function persist on a medium dose of ICS, or when it is desirable to reduce the current dose of ICS while maintaining optimal asthma control.⁵⁹

A systematic review of 10 RCTs demonstrated that the addition of a LABA to ICS therapy improves asthma symptoms, reduces exacerbations and permits a reduction in ICS maintenance dose.¹⁶⁸ Specifically, studies that compared reduced dose ICS/LABA combination to a fixed moderate to high dose ICS reported significant improvements in lung function and percent rescue free days with the ICS/LABA combination therapy. LABA permitted a reduction of 37% in patients on minimum maintenance ICS and up to 60% in patients on maintenance ICS without deterioration in asthma control. However, the review also found no significant difference in the number of severe exacerbations requiring oral corticosteroids when comparing the ICS/LABA combination to ICS alone. Another systematic review of 30 RCTs, published in the same year, compared ICS/LABA combination to a higher dose of ICS. This review reported similar findings, with significant improvements in lung function, symptom-free days and use of rescue SABA with combination therapy, but no significant difference in the rate of patients with exacerbations requiring systemic corticosteroids.¹⁶⁹ However, a third systematic review of 49 RCTs compared LABA to placebo in addition to ICS and reported a reduced risk of exacerbations with ICS/LABA combination therapy.¹⁷⁰ The addition of a daily LABA reduced the risk of exacerbations requiring systemic corticosteroids by 19% (RR 0.81, 95% CI 0.73-0.90). The number needed to treat for one extra patient to be free from exacerbation for one year was 18 (95% CI 13-33). Furthermore, it has been demonstrated that adding a LABA to an ICS is significantly more effective in increasing time with well controlled asthma when compared to increasing the ICS dose fourfold.¹⁷¹

In addition to their bronchodilator action, there is also evidence that LABAs have an anti-inflammatory and anti-remodelling effect on the airway in patients already taking ICS.^{172,173} Treatment of human lung fibroblasts and vascular smooth muscle cells with beta-2 agonists has been shown to cause enhanced movement of the glucocorticoid-glucocorticoid receptor complex from the cytoplasm into the nucleus, where it modulates gene transcription and exerts its anti-inflammatory action.¹⁷⁴

There is insufficient evidence at present to recommend use of combination ICS/LABA therapy rather than ICS alone as first-line treatment.¹⁷⁵ The NAC recommends a LABA should be the first choice for add-on therapy in patients whom adequate asthma control is not achieved despite low dose ICS treatment, after ruling out poor adherence and poor inhalation technique as causes.⁵⁹ In an attempt to improve adherence, devices are available combining ICS and LABA therapy in a single inhaler.

Currently, two ICS/LABA combinations are available in single inhalers. Seretide® contains fluticasone and salmeterol, and Symbicort® contains budesonide and eformoterol. Due to the increasing use of these combinations, a systematic review was recently performed on five RCTs (5,537 patients) to compare the relative effects of fluticasone/salmeterol and budesonide/eformoterol.¹⁷⁶ Lung function outcomes, symptoms, use of rescue medication, exacerbations requiring systemic corticosteroids, ED visits, hospital admissions and adverse events were not significantly different between treatments.

In light of the growing evidence that many patients neglect their preventer medication and over-rely on reliever medication, a new asthma management strategy has been evaluated in a series of clinical trials.¹⁷⁷⁻¹⁸⁰ The strategy utilises a single inhaler containing an ICS (budesonide) and a LABA with immediate onset of action (eformoterol) for both maintenance therapy and symptom relief. For patients with persistent asthma symptoms despite the regular use of ICS, studies have found that fewer severe exacerbations occurred with the maintenance and reliever regimen when compared to the conventional combination regimen of regular ICS plus a SABA when required. Table 5 summarises the results of COMPASS, the only published double-blind trial where the maintenance and reliever regimen was compared to a higher-dose conventional regimen.¹⁷⁷

Table 5. Rates of severe exacerbations in the COMPASS trial¹⁷⁷

Treatment group	Severe exacerbations per 100 patients per six months	Average daily ICS dose (budesonide equivalent)
Budesonide with eformoterol (maintenance and reliever regimen) (n = 1107)	12*	604 µg
Budesonide with eformoterol plus terbutaline as needed (conventional regimen) (n = 1105)	16	800 µg
Fluticasone with salmeterol plus terbutaline as needed (conventional regimen) (n = 1123)	19	800 µg

*The number of severe exacerbations was significantly less than with the budesonide with eformoterol conventional regimen ($P < 0.01$) and also significantly less than with the fluticasone with salmeterol conventional regimen ($P < 0.001$).

In August 2007, the Pharmaceutical Benefits Scheme listing of budesonide with eformoterol 100/6 µg and 200/6 µg (Symbicort®) was extended to allow Australians who experience frequent asthma symptoms while receiving combination ICS/LABA therapy or ICS alone to use the alternative budesonide with eformoterol maintenance and reliever regimen.¹⁸¹ The NAC has endorsed this new regimen (commonly called Symbicort® Maintenance And Reliever Therapy; SMART), with a SMART-specific written AAP now available.⁸⁰

1.6.5 Leukotriene receptor antagonists

According to current national⁵⁹ and international¹⁶ guidelines, ICS are the preferred anti-inflammatory medications for the treatment of persistent asthma. However, leukotriene receptor antagonists (LTRAs; montelukast and zafirlukast) may be an alternative treatment for mild persistent asthma. Placebo-controlled trials have demonstrated that LTRAs improve lung function, reduce symptoms and asthma exacerbations in adults¹⁸²⁻¹⁸⁴ and children.¹⁸⁵⁻¹⁸⁷

A systematic review of 27 RCTs found that LTRAs are less effective than ICS in adults with asthma. Patients treated with LTRAs were 65% more likely to suffer an exacerbation requiring systemic corticosteroids (RR 1.65, 95% CI 1.36-2.00).¹⁸⁸ In patients already on ICS, LTRAs cannot be substituted without risking the loss of asthma control.¹⁸⁹⁻¹⁹¹ While the addition of a LTRA to ICS therapy appears to be comparable to increasing the dose of ICS,¹⁹² a systematic review of 15 RCTs found that LABAs are more effective than LTRAs as add-on therapy.¹⁹³ The risk of exacerbations requiring

systemic corticosteroids was 17% lower with ICS plus a LABA when compared to ICS plus a LTRA (RR 0.83, 95% CI 0.71-0.97).

Clinical guidelines for adult patients, in accordance with safety and efficacy data, recommend that LTRAs be reserved as add-on therapy to ICS when LABAs are not tolerated, or when adequate control of asthma is not achieved with first line therapy.^{16,59}

1.6.6 Cromones

Cromones (cromoglycate and nedocromil) are anti-inflammatory agents that may be used as an alternative to ICS for the long-term treatment of asthma. Cromones have the advantage of having a well-established safety profile, with no significant adverse effects.¹⁹⁴

Although their efficacy is well-established in adults,¹⁹⁵ systematic reviews have casted doubt on the efficacy of cromones in children.^{196,197} The cromones appear to work best for patients who have mild asthma, although they are not effective for all such patients, and it is difficult to predict which patients will respond.¹⁹⁸ Therapeutic efficacy is usually obvious within one to two weeks but a four-week trial is recommended before considering other treatments.⁵⁹

A systematic review of 17 RCTs involving 1,279 children and eight RCTs involving 321 adults found that ICS were superior to cromoglycate on measures of lung function and asthma control for both adults and children with chronic asthma.¹⁹⁹ Among children aged 2 to 18 years, ICS were associated with a higher final mean FEV₁ (weighted mean difference 70 mL, 95% CI 20-110) and higher mean PEF (weighted mean difference 17.3 L/minute, 95% CI 11.3-23.3). In addition, ICS were associated with fewer exacerbations (weighted mean difference -1.18 exacerbations per year, 95% CI -2.5 to -0.21), lower asthma symptom scores, and less rescue bronchodilator use than cromoglycate. Among adults, ICS were similarly associated with a higher final mean FEV₁ (weighted mean difference 210 mL, 95% CI 130-280) and higher mean PEF (weighted mean difference 28.2 L/minute, 95% CI 18.7-37.6). ICS were also associated with fewer exacerbations (weighted mean difference -3.30 exacerbations per year, 95% CI -5.62 to -0.98), lower asthma symptom scores among cross-over trials but not parallel trials, and less rescue bronchodilator use than cromoglycate. When added to

ICS therapy, cromoglycate has shown little or no benefit,²⁰⁰⁻²⁰³ suggesting it is not effective as steroid-sparing therapy.

International guidelines state that the role of cromones in long-term treatment of asthma in adults and children is limited.¹⁶ Because their action is short, inhaled cromones must be used four times daily, an inconvenient regimen for long-term treatment. While there is a role for cromoglycate and nedocromil in the prevention of exercise-induced asthma,⁵⁹ they are less effective than SABAs.²⁰⁴

1.6.7 Methylxanthines

Asthma management guidelines recommend that theophylline can be used as add-on therapy to patients not controlled by low doses of ICS, but recommend LABAs as being more effective with fewer adverse effects.^{16,59} Theophylline may be indicated as maintenance treatment in patients with severe asthma who require multiple drugs to achieve symptom control.^{59,205}

There is evidence that theophylline has anti-inflammatory and immunomodulatory actions at lower plasma concentrations (5-10 mg/L).²⁰⁶⁻²¹⁰ However, these inflammatory actions do not render theophylline an alternative anti-inflammatory agent to ICS in asthma management, as several studies have shown that ICS have a more preferable risk/benefit profile than theophylline in the treatment in asthma.²¹¹⁻²¹⁵

Theophylline may be useful as add-on therapy to ICS in some patients. In patients with severe asthma, its benefits have been demonstrated by significant improvement in lung function and asthma symptoms after the addition of theophylline to high doses of ICS,²¹⁶ and by the worsening of lung function and asthma symptoms when theophylline is withdrawn, even when high doses of ICS or oral corticosteroids are continued.^{207,217-221} Studies have also reported a steroid-sparing effect of theophylline.²²² However, the role of theophylline in the treatment of asthma has declined, and has now been largely superseded by LABAs.⁵⁹

A systematic review of 12 RCTs (1,344 patients) found that LABAs, particularly salmeterol, are significantly more effective than theophylline, regardless of concomitant ICS use.²²³ While there was no significant difference between salmeterol and theophylline in FEV₁ predicted, salmeterol treatment led to significantly better morning PEF (mean difference 16.71 L/minute, 95% CI 8.91-24.51) and evening PEF (mean

difference 15.58 L/minute, 95% CI 8.33-22.83). Salmeterol also reduced the use of SABA, while eformoterol, used in two studies, was reported to be as effective as theophylline. Salmeterol was significantly less likely to produce central nervous system adverse events (RR 0.50, 95% CI 0.29-0.86) and gastrointestinal adverse events (RR 0.30, 95% CI 0.17-0.55) when compared to theophylline.

The soluble ethylene diamine salt of theophylline, aminophylline, was originally developed for intravenous administration and shown to be very effective in acute severe asthma, particularly in patients who had not responded well to adrenaline.²²⁴ However, in the management of acute asthma exacerbations, intravenous aminophylline has been superseded by the use of high doses of SABAs, as they are more effective and safer. Aminophylline does not appear to confer any additional benefit when added to SABAs and is now usually reserved for the rare patients with severe exacerbations who do not respond adequately to SABA therapy.²²⁵

The benefits of theophylline are limited by its toxicity. It has a narrow therapeutic index requiring dose titration and regular monitoring of serum concentrations to avoid adverse effects. Early pharmacokinetic studies demonstrated that the bronchodilator effect of theophylline was related to plasma concentration of 5-20 mg/L, but above 20 mg/L, adverse effects were very common.^{226,227} This led to recommendations for a therapeutic range of 10-20 mg/L. Theophylline is extensively metabolised in the liver by CYP1A2,²²⁸ thus drugs that inhibit this enzyme may increase plasma theophylline concentrations to levels that produce adverse effects.²²⁹ The most common adverse effects are headache, nausea and vomiting, abdominal discomfort and restlessness. There may also be increased gastric acid secretion, abdominal discomfort, gastroesophageal reflux and diuresis. At high concentrations, convulsions, cardiac arrhythmias and death may occur.²³⁰

1.6.8 Anticholinergics

Ipratropium and tiotropium are inhaled anticholinergic bronchodilators with a slower onset of action (30-60 minutes) than SABAs. Ipratropium has a duration of action of approximately four hours, whereas tiotropium's duration of action is close to 24 hours. The addition of ipratropium to a SABA has shown benefit in the initial management of moderate-to-severe asthma exacerbations.²³¹ A systematic review of 32 RCTs (3,611 patients) found significant reductions in hospital admissions in both children (RR 0.73,

95% CI 0.63-0.85) and adults (RR 0.68, 95% CI 0.53-0.86) who received inhaled anticholinergics combined with a SABA, compared to those receiving SABA alone in the emergency setting.²³² Combined treatment also produced a significant increase on spirometric tests at 60-120 minutes after the last treatment in children and adults.

The role of inhaled anticholinergics in the day-to-day management of asthma is limited. Systematic review evidence suggests that although ipratropium is better than placebo in adults with chronic asthma, the size of the effect is small.²³³ When used in combinations with a SABA, ipratropium does not appear to add much benefit. Available data has not shown any clear advantages of ipratropium over placebo in children with chronic asthma.^{234,235} While clear benefits of inhaled anticholinergics in the long-term management of asthma are yet to be established they are recognised as alternative bronchodilators for patients who experience such adverse effects as tachycardia, arrhythmia and tremor from beta-2 agonists.¹⁶

1.6.9 Anti-IgE treatment

Omalizumab is a recombinant monoclonal anti-immunoglobulin (Ig) E antibody approved for the treatment of patients with severe allergic asthma, who are already being treated with ICS and who have raised serum IgE levels.^{16,59,236} Elevated serum levels of IgE in response to common aeroallergens are a key component in the pathogenesis of atopic asthma.^{237,238} Omalizumab prevents free serum IgE from attaching to mast cells and other effector cells and prevents IgE mediated inflammatory changes.^{239,240} Studies in patients with atopic asthma showed that anti-IgE antibodies decrease serum IgE levels in a dose-dependent manner and allergen-induced bronchoconstriction during both the early and late-phase responses to inhaled allergen.^{241,242}

A systematic review of 14 RCTs (3,143 patients) demonstrated the efficacy of omalizumab in patients with mild-to-severe allergic asthma with high serum levels of IgE.²⁴³ Omalizumab was effective in reducing asthma exacerbations as an adjunctive therapy to ICS (OR 0.52, 95% CI 0.41-0.65), and during ICS tapering phases of clinical trials (OR 0.47, 95% CI 0.37-0.60). Treatment with omalizumab also significantly improved symptoms, quality of life and asthma control scores, and significantly reduced the requirement for rescue medication. In addition, omalizumab led to a significant reduction in ICS consumption compared with placebo (-119 µg per day, 95% CI

-154 to -183), and a significant increase in the number of patients who were able to reduce their dose of ICS by over 50% (OR 2.50, 95% CI 2.02-3.10) or completely withdraw their ICS (OR 2.50, 95% CI 2.00-3.13). However, the authors concluded that the clinical value of the reduction in ICS consumption has to be considered in the light of the high cost of omalizumab.

Approximately 5-10% of patients with asthma have severe disease that often fails to respond to conventional therapy, and these patients account for more than 50% of the total healthcare costs associated with asthma.²⁸ Several studies have demonstrated the cost-effectiveness of omalizumab for the treatment of severe allergic asthma, in patients who are not controlled with maximal conventional therapy.²⁴⁴⁻²⁴⁷ In patients who respond to therapy, the cost-effectiveness of omalizumab compares well to other biologic treatments for chronic illnesses.²⁴⁸ In Australia, omalizumab is not on the federally funded Pharmaceutical Benefits Scheme, and is estimated to cost each patient about \$23,500 a year for three injections per month.²⁴⁹ Reimbursement of pharmaceuticals in Australia is based on cost-effectiveness, and the usual process involves evaluation of clinical trial data for grouped subjects, with approval to use the drug based on eligibility criteria. While the cost-effectiveness for patients with severe allergic asthma in Australia has not yet been evaluated, small Australian studies have demonstrated that patients with difficult/therapy-resistant asthma respond well to omalizumab.²⁵⁰⁻²⁵² The studies raised a number of issues relating to the best method of using this treatment in such patients. In particular, the need to identify individual responders to omalizumab using single-patient controlled trials, rather than widespread use in patients with difficult asthma, was acknowledged. It is hoped that this approach represents an opportunity to balance rational prescribing with appropriate access to omalizumab in certain patients.²⁵⁰

1.6.10 Systemic corticosteroids

Systemic corticosteroids are useful for treating the airway oedema and increased bronchial secretions associated with the inflammation in acute asthma exacerbations.²⁵³ The early use of systemic corticosteroids delivered by either oral or intravenous routes during moderate-to-severe exacerbations is a principal treatment choice in asthma management guidelines.^{16,59} A systematic review of 12 RCTs (863 patients) determined that the early use (within one hour of arrival) of systemic corticosteroids for acute

asthma in the ED significantly reduced admission rates compared with placebo (OR 0.50, 95% CI 0.31-0.81), with the number needed to treat to prevent one admission being 8 (95% CI 5-21).²⁵⁴ This benefit was more pronounced in those not already receiving systemic corticosteroids (OR 0.37, 95% CI 0.19-0.70) and those experiencing a more severe exacerbation (OR 0.35, 95% CI 0.21-0.59). Adverse effects were not significantly different between corticosteroids and placebo, suggesting that ED treatment with systemic corticosteroids is safe. A separate analysis of six RCTs (374 patients) found that a short course (3-10 days) of systemic corticosteroids after ED discharge significantly reduced chances of a relapse (RR 0.38, 95% CI 0.20-0.74) without major adverse effects. The benefit lasted about three weeks.²⁵⁵ Further systematic review evidence on dosing schedules suggest that high-dose corticosteroids, at least in hospitalised patients, are no more effective than moderate and low doses.²⁵⁶

There is no evidence to suggest the advantage offered by systemic corticosteroids in moderate-to-severe asthma is related to the route of administration.²⁵³ Until further evidence is available, it is reasonable to select oral corticosteroids as the first-line choice while reserving intravenous corticosteroids for patients who are too dyspnoeic to swallow, are incubated or unable to tolerate oral medications.

In patients whose asthma exacerbation has not resolved despite an increase in ICS or combination therapy, a short course of oral corticosteroids of 40-50 mg given daily for 7-10 days, depending on the severity of the exacerbation, is recommended.^{16,59} When symptoms have subsided and lung function has approached the patient's best value, the oral corticosteroids can be stopped without tapering, provided that treatment with ICS continues.²⁵⁷ However, there is no evidence to suggest that prolonging the course beyond 10 days is indicated.²⁵⁷

Long-term oral corticosteroid therapy may be required for severely uncontrolled asthma, but its use is limited by the risk of significant adverse effects including osteoporosis, diabetes, hypothalamic-pituitary-adrenal axis suppression, obesity, cataracts, glaucoma and skin thinning.¹⁶ Systematic review evidence suggests that, in the management of adults with chronic asthma, a daily dose of prednisolone 7.5 mg/day appears to be equivalent to a moderate to high dose of ICS (300-2000 µg/day).²⁵⁸ Alternate-day doses of oral corticosteroids and doses less than 5 mg/day appeared to be less effective than low to moderate dose ICS. If oral corticosteroids have to be

administered on a long-term basis, the lowest effective dose should be prescribed, and attention must be paid to measures that minimise the systemic adverse effects.¹⁶

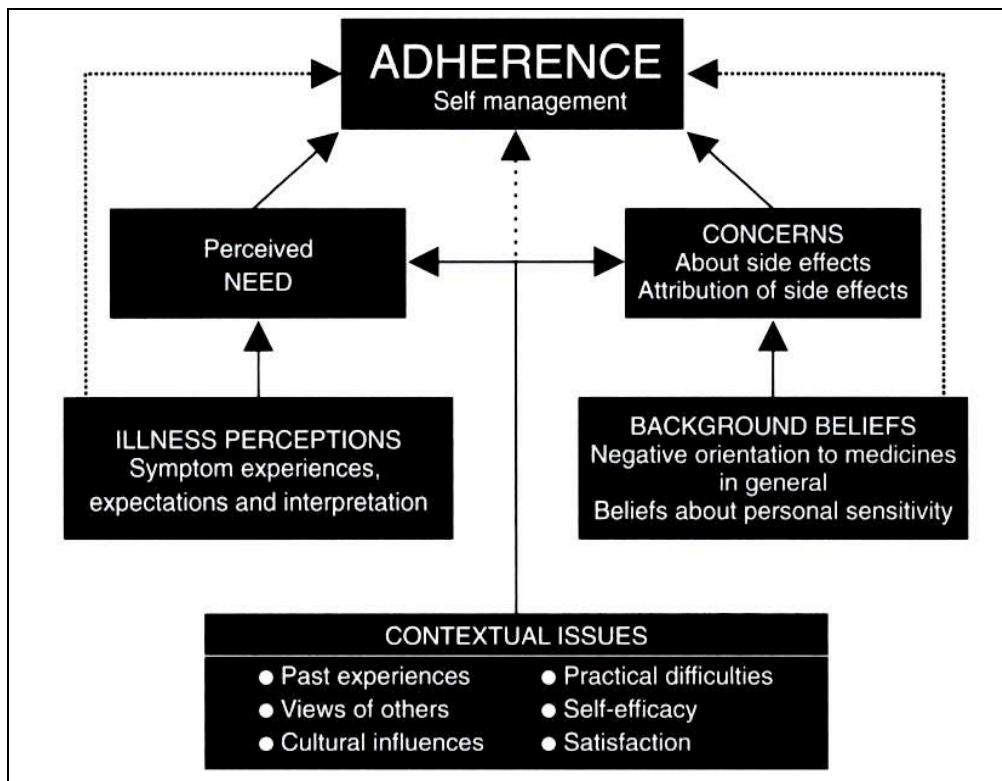
1.7 Barriers to optimal asthma management

1.7.1 Use of inhaled corticosteroids

Despite the overwhelming evidence that regular use of ICS improves health outcomes in patients with asthma, a National Health Survey highlighted evidence that the use of ICS, the cornerstone of drug therapy for asthma, is not well targeted. Many people who would benefit from ICS therapy were not doing so, with only 14% of people with current asthma reporting that they used their ICS every day or night in the previous two weeks. Furthermore, among people who were using SABAs every day (implying the presence of persistent asthma that is poorly controlled), only 37% also used ICS on three or more days per week and 60% did not use ICS at all.³¹

In asthma, as with other chronic conditions, poor adherence to treatment and medical advice is common.^{259,260} Barriers to ICS use must be overcome before widespread benefits of ICS therapy are seen. Patients' perception of their condition and their need for treatment limit the adherence to ICS therapy, and therefore the reported effectiveness of ICS. Patient adherence to medication is influenced by a number of factors relating to how the individual judges the necessity of their treatment relative to their concerns (Figure 8).²⁶¹ It has been reported that non-adherence to ICS therapy is strongly correlated with treatment beliefs, in particular, doubts about the necessity for medication to maintain health and concerns about the potential adverse effects.²⁶²

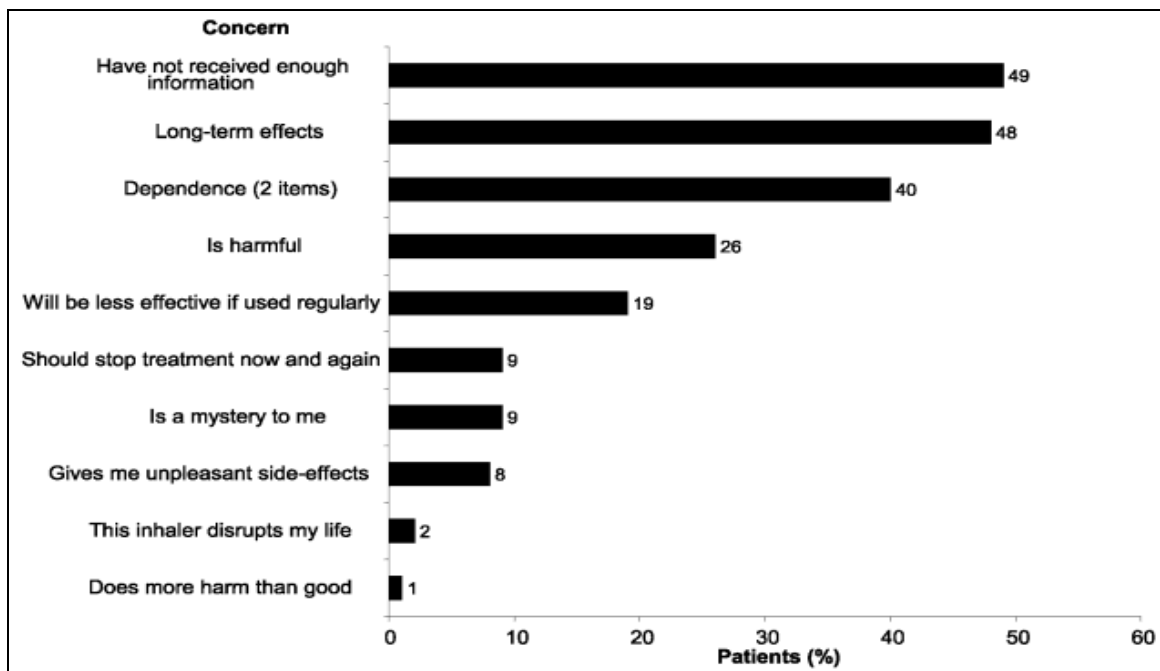
Figure 8. Factors influencing patient adherence to medication²⁶¹



It has been found that a large proportion of patients with asthma do not understand the role of their medications and have many misconceptions and fears in regard to ICS, reducing their willingness to use them.^{263,264} However, a review of articles regarding the safety of ICS concluded the following:

“ICS have minimal side effects in most patients when taken at recommended doses. The benefits of ICS therapy clearly outweigh the risks of uncontrolled asthma, and ICS should be prescribed routinely as first-line therapy for children and adults with persistent disease.”²⁶⁵

In addition to fear of corticosteroid-related adverse effects, it has been reported that factors such as the cost of medication, lack of symptoms, lack of immediate effect, and concern over long-term use of medicines and loss of effectiveness over time, might be important in contributing to the under-use of ICS.^{51,262,266-269} Figure 9 displays the degree to which variations in reported adherence to ICS could be explained by patients’ perceptions of asthma medication.

Figure 9. Common patient perceptions affecting ICS adherence²⁶²

Baiardini *et al.* showed how different factors may modulate adherence to asthma treatment.²⁶⁷ Relationships between treatment adherence and depression, anxiety and coping strategies were identified. The presence of anxiety was positively correlated with fear of medication adverse effects and difficulty in accepting the illness, and negatively correlated with acceptance of illness limitations. The presence of depression was negatively correlated with acceptance of illness limitations, knowledge of illness and the ability to identify worsening signs.²⁶⁷ The authors concluded that general difficulties, fears, perspectives and resources, if neglected, might result in barriers that diminish asthma control. The findings suggest that identifying motivations behind non-adherence may result in more effective patient-focused care and improved asthma outcomes.

The Australian Centre for Asthma Monitoring examined patterns of asthma medication use in Australia, and reported that people living in remote areas use asthma medications less often than people living in cities, which may reflect differences in the accessibility of healthcare services. Furthermore, people with concession cards, who are able to purchase medications at a much cheaper price than general patients, use ICS and LABAs more often than general patients, which raises the possibility that the price charged to general patients represents a barrier to the use of preventive medications for asthma.²⁷⁰

An Australian qualitative study exploring the burden of asthma on the lives of people presenting to hospital EDs found that the cost of asthma medication was an issue for nearly two-thirds of patients.²⁷¹ Some participants performed their own 'cost-benefit' analysis, weighing up expense, perceived adverse effects and potential benefits of their medications. As a consequence, a significant proportion chose to alter medication doses, in an attempt to prolong medication use, or to not take prescribed medications. The authors concluded that to achieve a therapeutic partnership, doctors need to be aware of the substantial social, personal and financial burden of asthma for their patients, and should recognise that patients' perceptions of treatment cost may compromise treatment adherence.

Patients require constant reinforcement when provided with information as they tend to forget or are unable to recall pertinent facts, which may then impact on their adherence to medication and overall satisfaction.²⁷² It has been demonstrated that instruction and demonstration can have a large impact on the percentage of patients who use an inhaler correctly.²⁷³ Failure to instruct patients on how to use inhalers and to reinforce these instructions will decrease adherence, whatever the drug or inhalation device. Poor inhalation technique ultimately represents a form of unintentional non-adherence and can be easily overcome by close monitoring and continuing education by the healthcare professional.

Inadequate use of ICS could be due to under-prescribing and/or poor adherence with therapy. It has been suggested that the major reason that GPs fail to prescribe ICS is disagreement with recommendations, particularly regarding where the balance lies between their benefits and the risk of complications and adverse effects.²⁷⁴ The implementation of best practice guidelines for asthma management requires not only insights into the perspectives of those living with asthma, but also an understanding of what GPs' priorities are for achieving optimal outcomes in people with asthma, and the barriers they face in delivering this care. Goeman *et al.* conducted a qualitative study asking GPs what their main concerns were for achieving best outcomes in people with asthma.²⁷⁵ The GPs in the study identified both structural and knowledge barriers. These included the time required and the cost of providing asthma management and patient education, as well as accessing relevant continuing medical education. Tumiel-Berhalter *et al.* showed that knowledge of GPs and their attitudes towards asthma management guidelines were associated with regular use of anti-inflammatory asthma medication.²⁷⁶

These findings reinforce the view that GP-perceived usefulness is critical to implementing asthma guidelines and ensuring adequate prescribing of ICS.

1.7.2 Use of Asthma Action Plans

National guidelines for the management of asthma consistently recommend that all patients with asthma should have an individualised written AAP.⁵⁹ Most Australians with asthma, however, do not have AAPs.^{3,31,46-49} Findings from the 2004-05 National Health Survey showed that while there has been an improvement on the rate of possession of an AAP since 2001, less than one-quarter (23%) of people with asthma possessed a written AAP in 2004-05, and approximately 5% of people with asthma had never heard of an AAP.³¹

While there is strong evidence for the effectiveness of written AAPs, especially in combination with education and regular review, for this evidence to translate into practice both the GP and the patient need to be willing to participate. It has been shown that the most common reason for not possessing an AAP was simply that the patient had not been given one by his or her doctor.²⁷⁷ A study which sought to identify factors associated with uptake of the Asthma 3+ Visit Plan (which incorporates development of an AAP) found that GP workload, paperwork and perceived administrative burden were major factors to implementing the plan.²⁷⁸

A qualitative study of views of health professionals and patients on guided self-management plans for asthma found that health professionals worried about ‘blind obedience’ with self-management plans. Concern was expressed that patients would rely on a written plan and not return for regular review, or that the plans ‘encouraged dependency.’ All GPs tended to agree that the plans were difficult to implement in everyday practice given the constraints of time and tended to militate against a meaningful doctor-patient relationship.⁷⁵

A confounding factor of AAP possession is whether patients actually use their plans. Douglass *et al.* found that not all patients with an AAP used it, and that scores for asthma knowledge did not differ between those who had an AAP and those who were not confident to use it.²⁷⁷ This finding demonstrates that there are indeed other patient barriers to the use of an AAP. Interestingly, Jones *et al.* reported the following:

“Many patients with mild-to-moderate asthma do not regard it as a chronic disease that needs regular monitoring and therapeutic adjustments. Indeed, they prefer to manage it as an intermittent acute disorder, and they are uncomfortable with a guided self-management plan that reinforces asthma as a chronic, ongoing disease needing monitoring and managing.”⁷⁵

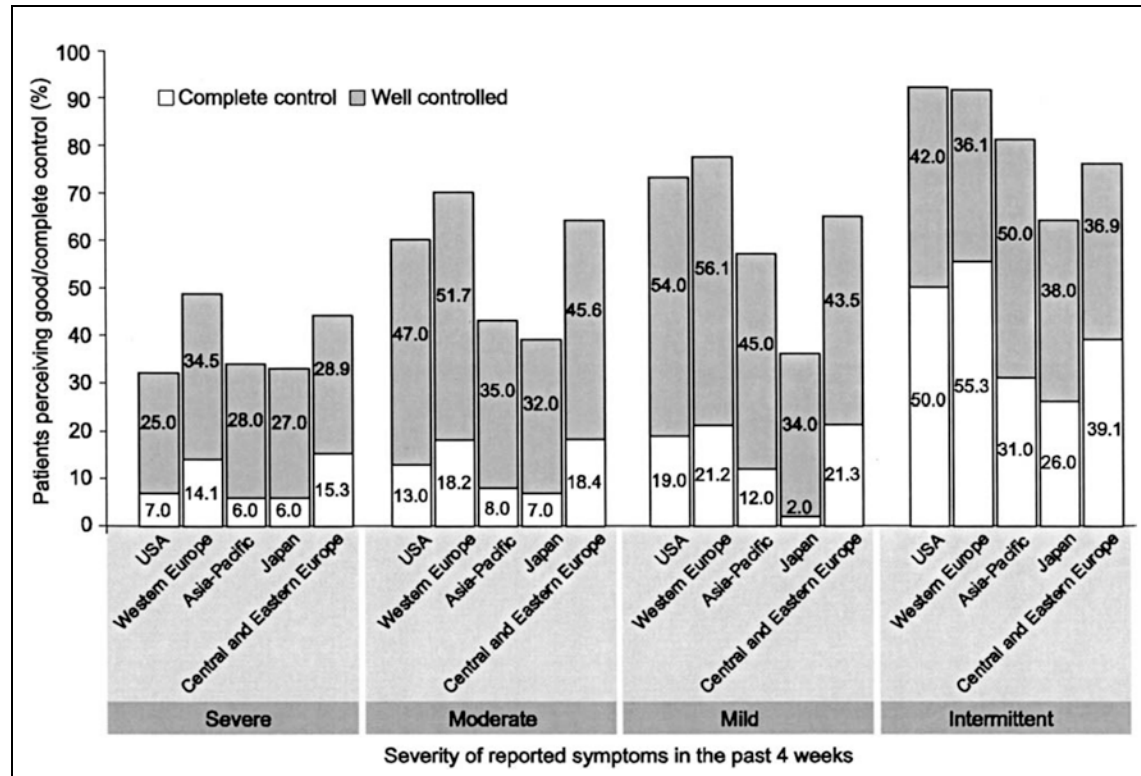
Patients’ preference to treat their asthma as an acute disorder is a common finding,⁷⁵⁻⁷⁷ and represents a clear barrier to patient-implementation of AAPs. The NAC therefore promotes the concept of patient-centred healthcare,²⁷⁹ a system designed to respect the patient’s preferences, values and needs.²⁸⁰ The concept aims to facilitate a shift from a medical model to a patient-centred healthcare model through enhancing patients’ and carers’ roles. Patient-centred healthcare recognises that human behaviour influences outcomes, and that chronic conditions with complex management require more complex means of interaction with the patient to ensure adherence to agreed treatment plans and improved QOL and clinical outcomes.²⁸⁰ It has been reported that most patients with AAPs modify them according to their perceptions of asthma severity and likely disease outcome.²⁷⁷ Therefore, to facilitate the implementation of a prescribed action plan, healthcare providers need to acknowledge and include the patient’s personal experience of their disease. It is hoped that this shift towards a more patient-centred approach to asthma management will improve the prevalence of AAP possession and implementation by increasing patient participation, as this has been shown to be associated with improved asthma management.⁸¹

1.7.3 Perception of asthma control

A well-documented patient barrier to optimal asthma management and control is an underestimation of disease severity on the part of the patient.^{46,51,52,55,281,282} Patients may unnecessarily accept symptoms, assuming that frequent symptoms, exacerbations and lifestyle limitations are an inevitable consequence of having asthma.⁵¹ In the Asthma Insights and Reality in Europe study, only 5% of adults met all the criteria for asthma control as defined in the GINA guidelines, but 66% of adults considered that they had no asthma symptoms or had only mild asthma.⁵² Globally, surveys have indicated that 32-49% of patients experiencing severe symptoms and 39-70% of patients with

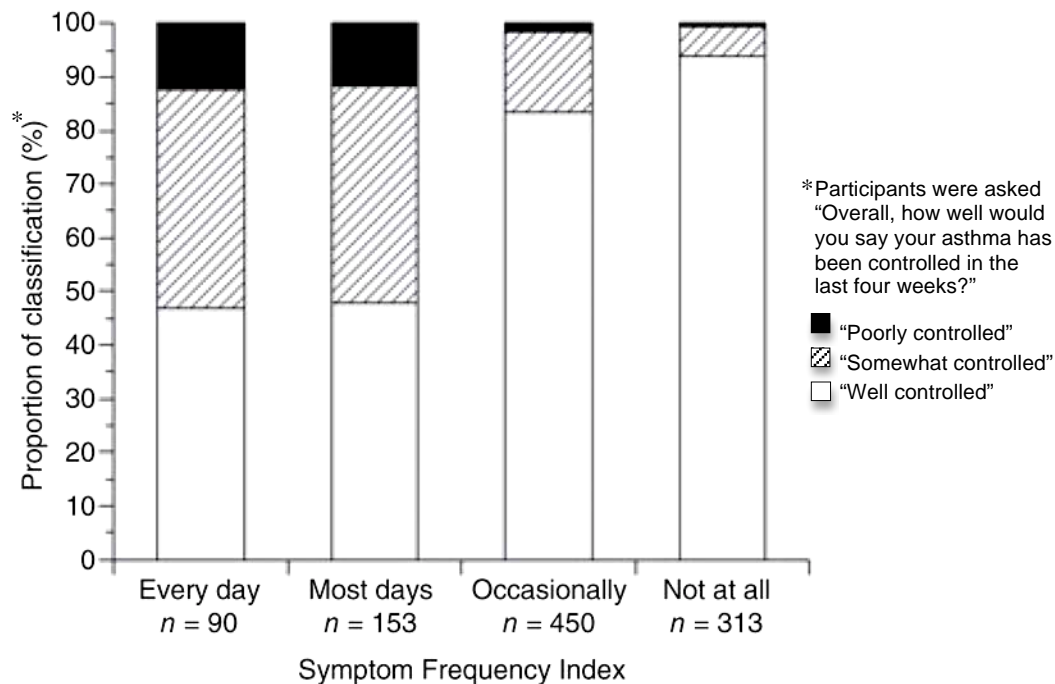
moderate symptoms believe that their asthma is well controlled or completely controlled,⁵⁵ as shown in Figure 10.

Figure 10. Patients' perception of asthma control against actual symptom severity among regions⁵⁵



A nation-wide study aiming to assess the burden of asthma and describe asthma management in Australia reported low rates of effective asthma therapy use, including in those with features of poor asthma control.⁴⁶ Furthermore, there was discordance between the classification of asthma control, on the basis of reported symptom frequency and asthma management guidelines, and patients' own evaluation of how well their asthma had been controlled. Many patients who reported frequent symptoms regarded their asthma as 'well controlled.' In fact, nearly half the patients with daily asthma symptoms responded in this way and only a small minority reported that their asthma was poorly controlled (Figure 11).

Figure 11. Self-assessment of asthma control by symptom frequency index among participants of an Australian study⁴⁶



Interestingly, poor perceptions of asthma control can be a problem in GPs as well as their patients. A recent practice audit of Canadian GPs attempted to address the gap between asthma control achieved and asthma control achievable.²⁸³ Of the 10,428 patients assessed by 354 GPs, 59% were uncontrolled, 19% well controlled and 23% totally controlled. GPs overestimated control, regarding only 42% uncontrolled. Additionally, GPs were found to be discordant with guideline classification of asthma control in 31% of uncontrolled patients, 13% of well-controlled patients and 2% of totally controlled patients. Most commonly, GPs were discordant with guideline criteria when patients showed a lack of control in only one parameter, most often the overuse of reliever medication.

The 2005 International Control of Asthma Symptoms (ICAS) survey of patients and GPs found that despite the majority of patients being seen by GPs having mild-to-moderate asthma, most patients reported an absence of asthma control and many reported significant lifestyle restrictions.²⁸⁴ The findings corresponded with high levels of concerns amongst GPs that patients accept their symptoms as normal, and frustration that their patients were not more forthcoming about their symptoms. These findings suggest that too many patients have symptoms that they accept as being a normal consequence of their condition and many rely heavily on their rescue medication.

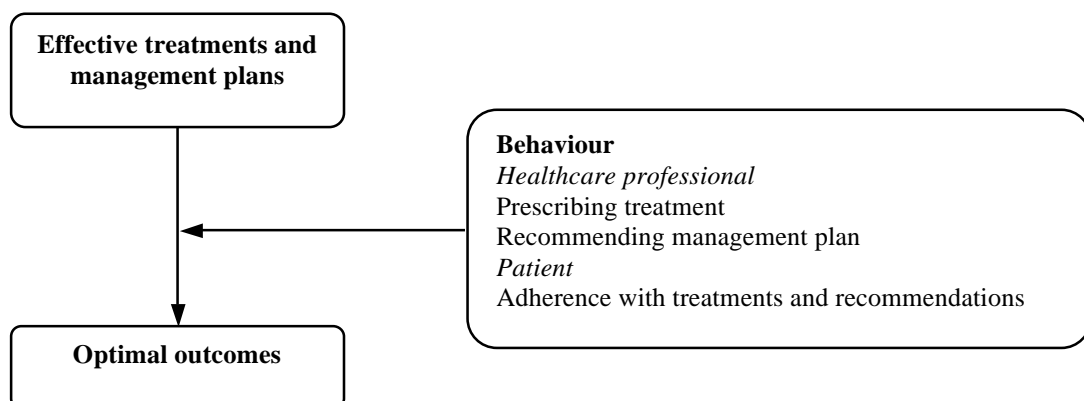
Indeed, patients' underestimation of asthma severity has been shown to result in inappropriate medication use.²⁸⁵

The results of the ICAS survey emphasised that action is required to encourage patients to view their asthma more seriously and to be more proactive in reporting symptoms to their GP. These actions, coupled with greater prompting of patients by GPs and other health professionals about their asthma, should help to optimise asthma management. These findings are consistent with other research suggesting that patients prefer to manage their asthma as an acute intermittent disorder rather than a chronic ongoing disease that needs monitoring and managing.⁷⁵⁻⁷⁷

1.7.4 Relationships with healthcare professionals

There are many possible reasons for suboptimal asthma control. However, regardless of the underlying causes, the level of control achieved reflects the behaviour of both healthcare professionals and patients (Figure 12). Differences in the perspectives of patients and healthcare professionals could affect their behaviours, and consequently, the achievement of asthma control. It may be possible for healthcare professionals to improve asthma control by achieving a greater understanding of the patient's perspective.²⁸⁶ An Australian study found that GPs often have relatively poor insights into self-management practices, even in high-risk patients.²⁸⁷ The authors concluded that this should be considered when planning future campaigns to improve asthma management and further reduce mortality.

Figure 12. Patient and healthcare professional behaviour affects asthma control²⁸⁶



Patterns of provision of healthcare, including non-specialist care, have been described in various populations as important factors affecting the use of asthma medication. Adams

et al. sought to examine the influence of patterns of care delivery and prescriber behavioural factors on the use of anti-inflammatory medication by patients with asthma. Being under the care of respiratory specialists, having regularly scheduled GP visits for asthma, possession of a written AAP and possession of private health insurance were all found to be significant indicators for ICS use for asthma.²⁸⁸

Effective communication between GPs and patients is integral for asthma management to be successful. An Australian qualitative study of patient language about worsening asthma found that there were important differences in the language patients and GPs used to describe worsening asthma.²⁸⁹ ‘Attack’ was the most commonly used word in asthma, and while it is simple and evocative it is limited in its utility, as patients used it for a wide spectrum of episodes. Furthermore, it was found that social context strongly influenced patients’ choice of language; patients commonly downplayed the severity of episodes to avoid causing alarm or attracting criticism. Such behaviour may be hazardous, as it could cause delays in obtaining medical assistance. The findings clearly highlighted gaps in language about asthma. Without readily understood and unambiguous words for the use in educational material and AAPs, communication breakdown may occur, impeding appropriate and timely management of worsening asthma. The authors concluded that healthcare providers should be encouraged to establish a relationship with patients in which patient language is understood and reflected back by the provider, to ensure effective communication about worsening asthma.²⁸⁹

Moffat *et al.* reported that poor healthcare professional-patient communication seems to largely explain the poor uptake of best practice guidelines in general practice and primary care.²⁸² In particular, healthcare professionals reported lacking the necessary communication skills for dealing with patient asthma control issues, particularly where these were non-medical (for example, identification of patients’ health beliefs and confidence in managing their own asthma and relevant non-medical lifestyle factors impacting on control). There is clearly a need to identify key communication skills for effective healthcare professional-patient partnerships in asthma management.

Aside from effective communication with patients, a good doctor-patient relationship is essential for achieving asthma control. Achieving a ‘therapeutic partnership’ has a major influence on optimal health outcomes and patient satisfaction.^{290,291} It has been

demonstrated that patients who rate their GP more highly in terms of ability to explain asthma management, willingness to spend time with the patient and encouragement to participate in treatment decisions, report ICS use significantly more often than patients with less favourable ratings of their GP's behaviour.²⁸⁸ It is frequently assumed that patients presenting to hospital EDs with asthma do not have good GP-patient relationships, or may not even have a GP for asthma care.²⁹² Douglass *et al.* performed a qualitative study examining the nature of patients' relationship with their GPs in those presenting to hospital EDs for asthma care.²⁹³ While nearly all the patients enrolled in the study had a GP whom they saw for their asthma, the findings identified that perceptions of GPs' competence, ability to listen and time constraints were important influences on GP-patient relationships. Participants expressed feelings of being rushed or wishing that the GP had time to sit and listen, and they expected the GP to be respectful of their own knowledge and experience of disease. The findings led the authors to urge GPs to ascertain patients' expectations of consultations and to respect a patient's interpretations of their symptoms and disease experiences in order to achieve a therapeutic partnership.²⁹³

The Global Asthma Physician Patient (GAPP) survey was designed to uncover asthma attitudes and treatment practices among separate groups of GPs and patients, with the goal of identifying barriers to optimal management.²⁹⁴ Findings of the GAPP survey revealed that there was a direct relationship between the quality of GP-patient communication, the level of adverse effects from medication and the extent of patient adherence. Furthermore, patient education on their disease and treatment was identified as a major barrier to optimal asthma management. Patient responses revealed a low level of asthma education, and this had a negative impact on treatment outcomes. However, patient education is unlikely to improve outcomes unless it allows patients to improve their self-management skills, as it has been demonstrated that programs that offer knowledge without self-management skills do not reduce hospitalisation rates or urgent GP visits.^{72,73}

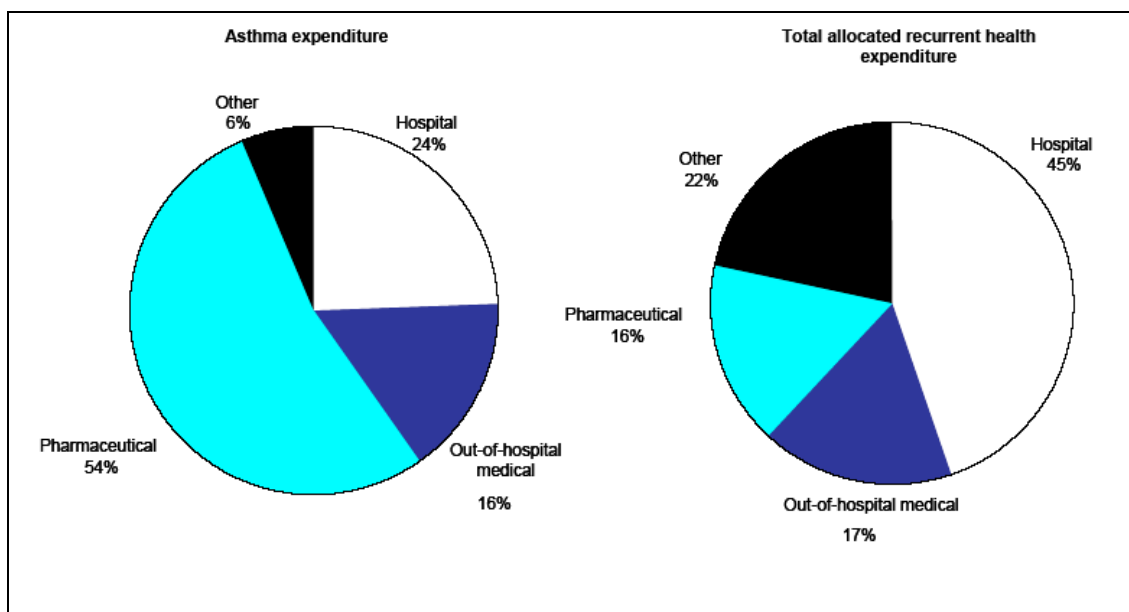
1.8 The pharmacist's role in asthma management

Community pharmacists are in a unique position to help patients manage chronic diseases in view of their expertise, their regular contact with patients and their accessibility. Pharmacists frequently see patients with asthma in the community, many

of whom may have suboptimal asthma control. Community pharmacies therefore represent an excellent site to screen for patients who may be at risk from their asthma and to address critical issues in asthma management in the community.

The Australian Centre for Asthma Monitoring reported that over half of all asthma expenditure is attributable to pharmaceuticals (Figure 13).³³ Indeed, every year Australian pharmacists fill more than seven million prescriptions for asthma medications, which remain the principal treatment for the disease.²⁹⁵

Figure 13. Distribution of asthma and total allocated recurrent health expenditure among health sectors, Australia, 2000-01³³



When dispensing prescriptions for asthma medication, pharmacists can play a pivotal role in educating patients about their therapy and condition (Table 6). This may be particularly important for encouraging adherence to ICS therapy, even when no symptoms are present.

Table 6. Actions for pharmacists to improve asthma management^{296,297}

1. Educate patients about asthma medications
2. Instruct patients about the proper technique for inhaling medications
3. Regularly review the patient's dispensing history to assess medication adherence
4. Encourage patients regularly purchasing non-prescription asthma relievers to see their GPs
5. Help patients use peak flow meters appropriately
6. Educate patients with persistent asthma on the importance of regular ICS therapy, taking time to reassure them that the benefits of ICS therapy outweigh the risks of uncontrolled asthma
7. Ensure that patients know how to recognise worsening asthma and what to do in such a scenario.
8. Encourage patients to ask their GP about developing an AAP if they do not have one already
9. Help patients understand their asthma management plans
10. Ask patients to complete an asthma control test while they are waiting for their prescription, discuss their results and refer if necessary

As members of the healthcare team, pharmacists can help improve the pharmacological management of asthma by teaching patients about their medications, how to use them and the importance of using them as prescribed. Alerting GPs to suspected problems, such as under-using ICS therapy or over-using relievers, will provide an opportunity for the GP to consider changes in a patient's management plan when appropriate.^{296,298}

A review of international literature from 1997 to April 2008 revealed a substantial increase in outcome-based asthma management programs that include the services of a pharmacist.²⁹⁹ The considerable increase in the number of research reports supporting pharmaceutical care in patients with asthma is consistent with the expanding role of pharmacists in this field in all parts of the world. Over the last decade, pharmacists have been active in asthma education in the community via various approaches. Examples of some activities include small group education to asthma patients in various settings, education to nurses about asthma, promotion of asthma awareness through fund-raising and participation in local and national organisations.

Studies conducted in Australia indicate that pharmacists are well placed to deliver interventions to improve asthma control and health outcomes, and patients report high levels of satisfaction with such services.^{5,300-304} The largest Australian pharmacy-based asthma intervention study assessed the impact of a pharmacy asthma care program (PACP; an ongoing cycle of assessment, goal setting, monitoring and review).³⁰¹ Fifty pharmacies participated in the study, half of which implemented the PACP, while the

other half provided usual care to control patients. The intervention resulted in improved asthma control, improved adherence to preventer medication, decreased mean daily dose of reliever medication, a shift in medication profile from reliever only to a combination of preventer, reliever \pm LABA, as well as improved scores on risk of non-adherence, QOL and perceived control of asthma questionnaires. The authors concluded that while the study showed that community pharmacists can add value to the care of asthma in terms of clinical and humanistic outcomes, further research is required to determine which components of the service are critical to improve asthma control and to determine the intensity of the service required to sustain the improvement.³⁰¹

Despite the efforts of the NAC in propagating their best practice guidelines, they are still not widespread in practice. One of the barriers reported by pharmacists in intervening successfully is their lack of sufficient knowledge.^{305,306} In a survey conducted with a sample of 1,610 Australian pharmacists by the Victorian College of Pharmacy and the NAC, practicing pharmacists' knowledge about asthma was not adequate.³⁰⁷ Well-designed educational strategies are required to encourage health professionals to understand and adopt best practice guidelines into everyday practice.

An Australian study was designed to bridge the gap between the ideal and reality of what is achieved in community pharmacies and addressed the training needs of community pharmacists with an educational program.³⁰⁸ In the intervention area, 15 pharmacies were trained with the educational intervention, and they provided specialised asthma care to 52 patients over six months, while in the control area, 12 pharmacists provided usual care to 50 patients. The intervention pharmacists were highly satisfied with the education received and rated most aspects highly. Improvements in patient clinical, humanistic and economic outcomes in the intervention group were obtained.

A Canadian pilot study evaluated the impact of an asthma continuing education program on community pharmacists' knowledge and interventions, as well as the appropriate use of asthma medications among patients.³⁰⁹ Whilst pharmacists' knowledge improved after the continuing education program, the number of interventions reported during the six-month period following the program was low and did not differ significantly compared to the control group of pharmacists. Furthermore, the appropriateness of asthma medication use among patients did not improve once the continuing education

program had been completed. The authors suggested that other identified barriers may have explained why pharmacists did not intervene more frequently. Possible impediments to a pharmacist's intervention to improve asthma management have been identified, and include difficulties in contacting GPs, attitudes of GPs towards pharmacists, lack of time, insufficient technical support, absence of a confidential consulting area and lack of patients' cooperation.³¹⁰

An Australian study in rural New South Wales was designed to address the issue of asthma awareness in a rural community and the involvement of the community pharmacist in proactive health promotion. The study reported that pharmacists demonstrated an overwhelming enthusiasm for their role in health promotion.³¹¹ Training enabled them to overcome their personal barriers, lack of confidence and resistance to a new concept. It was also reported that most of the pharmacists involved in the study continued with asthma services and have since been providing comprehensive disease state management in their community.

With patients frequently visiting pharmacies for prescription refills, community pharmacists are in an ideal position to identify medication-related problems that may impede optimal asthma management. A specialist asthma service offered by community pharmacists was evaluated in New Zealand over a two-year period.³¹² For the 100 patients enrolled in the trial, an average of 4.3 medication-related problems were identified per patient, with two-thirds of these compliance-related. The most common interventions were revision of patients' AAPs, referral and medication counselling. The benefits of this service included reduced reliever use and improved symptom control in around two-thirds of patients.

A rigorous evaluation of community pharmacist involvement in asthma management was conducted in the United States (US), which compared patients receiving pharmaceutical care (including education and peak flow monitoring) to a control group that received peak flow monitoring alone and another control group that received usual care.¹⁰ Although improvement in PEF was better in the intervention than in the usual care group, it was no better than in the peak flow control group. Furthermore, there were no differences among the groups in pre- and post- intervention improvement in QOL or medication adherence. It was concluded that providing a peak flow meter to patients

with asthma improved respiratory function, but that pharmaceutical care provided no incremental benefit.

An important lesson from this study was that the relatively intensive program had a poor uptake and implementation by pharmacists, and this was the most likely explanation for the somewhat disappointing findings.¹⁰ Despite the intensive efforts by the investigators in designing a pragmatic program and reinforcing its use, it was not used consistently. The pharmacists only viewed the data in the study computer half the time patients filled prescriptions, and they documented interventions only 50% of the time that those records were viewed. Thus, the intended intervention was not implemented often, presumably because of time constraints.

While there clearly is the potential for community pharmacists to have an impact in improving the management of asthma, such approaches are most likely to be successful if they do not require significant time and training on the part of the pharmacist. The authors of the US study concluded that additional research evaluating interventions to improve asthma management should be conducted in ‘real-world’ community pharmacies using strategies that are pragmatic in busy pharmacies.¹⁰

1.9 Data mining dispensing records to perform asthma interventions

In the pilot research leading up to the work described in this thesis, researchers at the Tasmanian School of Pharmacy developed a ‘data mining’ software application (‘MedeMine’) that seamlessly extracts data from the market-leading pharmacy dispensing software system in Australia (Fred Dispense; Fred Health).⁵ About 50% of community pharmacies in Australia use this dispensing system. The software application was designed to assist community pharmacists to use their medication records to identify people who may have poorly controlled asthma. It was intended to trial a computer-assisted intervention requiring minimal time and training on the part of the pharmacist, yet answering the societal need for improved asthma management. In October 2006, forty-two pharmacies throughout Tasmania participated in a pilot study, and used the software application to data mine dispensing records and generate a list of patients who had received three or more canisters of SABA in the preceding six months. Identified patients were randomised to an intervention or control group. Intervention patients were contacted by the community pharmacy via mail, and sent an intervention pack consisting of a personalised letter suggesting a visit to their GP for a review of

their asthma management, educational material from the Asthma Foundations Australia ('Asthma: the basic facts'³¹³), questionnaires assessing asthma knowledge, asthma control and asthma-related QOL, and a letter and questionnaire to hand to their GP. Control patients received no active intervention during the data collection phase other than the pharmacist's usual care. All patients were given asthma-related questionnaires six months later (April 2007). Due to ethical considerations, control patients were sent an intervention pack at this stage, similar to that sent to intervention patients six months earlier. Thirty-five pharmacies completed the project, providing 702 intervention and 849 control patients. The primary outcome measure was the ratio of dispensed preventers (ICS) to dispensed relievers (SABAs), and secondary outcome measures were other patterns in dispensed asthma medication (e.g. LABAs) and asthma questionnaire scores.

The intervention resulted in:

- A three-fold increase in the preventer-to-reliever (P : R) ratio ($P < 0.0001$);⁵
- A shift in medication profile from reliever only to a combination of ICS \pm reliever \pm LABA ($P < 0.01$);⁵ and
- Significant improvements in self-reported asthma control ($P < 0.001$) and asthma-related QOL ($P < 0.05$).³⁰⁴

Satisfaction with the intervention was encouraging among all participants, with the majority of GPs, pharmacists and patients agreeing that this type of program would improve asthma care in the community if implemented on a larger scale. The intervention seemed to be pragmatic in its implementation with more than 90% of pharmacists agreed that the MedeMine program was easy to use and that the project required a minimal amount of their time.

A number of pharmacists who participated in the pilot study indicated that they would prefer to hand out the intervention material to patients face-to-face, rather than mail the packs out. This highlighted the need for finding a balance between interventions that are pragmatic for busy community pharmacies, which require minimal disruption to the pharmacist's workflow, whilst encouraging and supporting the involvement of the pharmacist in the delivery of the intervention.

It was concluded that the intervention should be followed-up to determine whether the improvements in asthma management are sustainable, and varying levels of pharmacist interventions should be trialled on a larger scale. The asthma research described in this thesis expands on the aforementioned pilot study. In order for this type of study to be implementable on a national scale, the sustainability, feasibility and likely uptake by pharmacists, GPs and patients needed to be determined.

CHAPTER TWO:

SUSTAINABILITY AND FEASIBILITY OF A COMMUNITY PHARMACY INTERVENTION TO IMPROVE THE MANAGEMENT OF ASTHMA

2.1 Aim and objectives

This study aimed to determine the sustainability and perceived feasibility of a multidisciplinary intervention that utilised community pharmacy dispensing records to identify and educate patients with suboptimal asthma management. Specifically, the objectives were to:

- Determine the long-term effect of the intervention on the ratio of dispensed asthma preventer medications to dispensed asthma reliever medications;
- Determine the optimum frequency of the intervention to gain sustained improvements;
- Determine patient, community pharmacist and GP perceptions regarding the intervention;
- Determine the barriers and enablers to the national implementation of a best-practise intervention; and
- Determine what practice changes are required to successfully implement the intervention on a national scale.

2.2 Methods

2.2.1 Study design and setting

This project was a follow-up to a pilot study that was conducted in 2006-07. Briefly, the pilot study involved the utilisation of a software application that data mined community pharmacy dispensing records to identify patients who had received three or more canisters of SABAs in the six-month pre-intervention period. A multidisciplinary educational intervention was implemented, that referred such patients to their GP for a review. De-identified and uniquely coded dispensing data was collected at the end of a six-month post-intervention period to determine the impact of the intervention on the ratio of dispensed ICS to dispensed SABAs.⁵

The present study involved both quantitative and qualitative approaches. Firstly, a follow-up of the intervention was conducted to determine whether the improvement in asthma management was sustained. Secondly, qualitative interviews were conducted with patients, community pharmacists and GPs, to determine the perceived feasibility of the community pharmacy intervention. The study was conducted in Tasmania, Australia.

2.2.2 Quantitative component

2.2.2.1 Recruitment of pharmacies

Community pharmacists who participated in the previous asthma intervention were informed about the follow-up study by telephone. Each pharmacy was offered a \$50 honorarium for participating in the follow-up project. With the pharmacists' consent, each pharmacy was visited and the modified version of the data mining software was installed on the main dispensing computer.

2.2.2.2 The data mining software

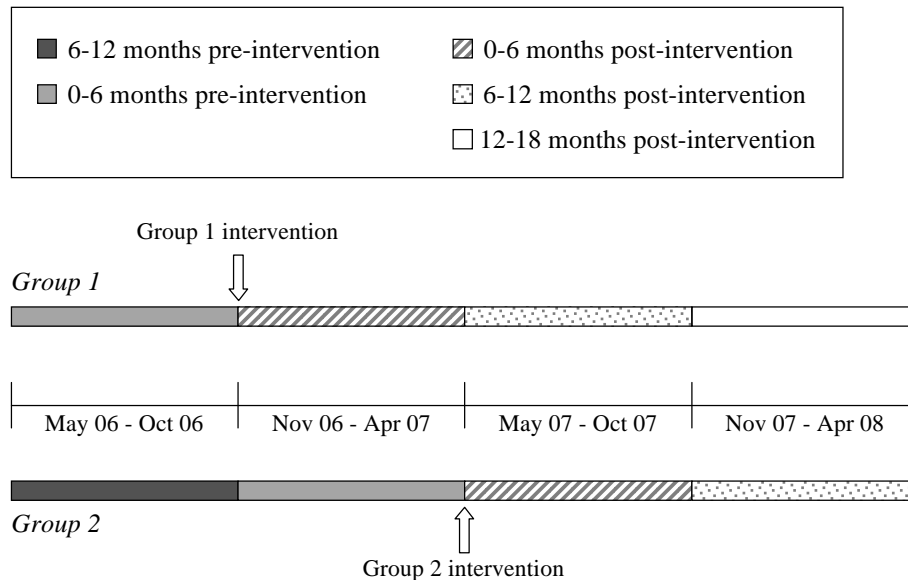
The information technology development under this study involved modifying the existing data mining software application so that it could re-identify patients who were targeted for an intervention in 2006-07. This would allow for the follow-up dispensing data for all patients to be compared to their pre- and post- intervention data collected originally. Each patient was uniquely coded to enable this. Upon installing the updated software on a pharmacy's dispensing computer, the dispensing data was de-identified, compressed and encrypted using a blowfish algorithm.³¹⁴ The information was then transferred via the Internet using a secure 1024 bit transfer protocol to a secure server at the University of Tasmania. Back-ups of the encrypted, de-identified data were also copied to a portable USB device.

2.2.2.3 Study population

The original intervention was a controlled study design. The data mining software identified patients who had received three or more canisters of asthma reliever medication in the six-month pre-intervention period, and randomised patients to an intervention or control group. For ethical reasons, control patients received an intervention at the end of the six-month post-intervention period, if they had again received three or more relievers in this time period. Therefore, the follow-up data

analysis described here was not controlled, and consequently the original intervention and control groups were referred to as Group 1 and Group 2, respectively. For the purposes of this study, the time periods are shown in Figure 14.

Figure 14. Timelines for dispensing data analysis



2.2.2.4 Handling of data and statistical analysis

The asthma medications included in the analyses were inhaled SABAs (relievers) and ICS (preventers). Prior to performing statistical analyses, the dispensed quantities of asthma medications were converted to a standard equivalent dose:

- Salbutamol equivalence: salbutamol 100 µg = terbutaline 250 µg;³¹⁵ and
- Beclomethasone-HFA equivalence: beclomethasone-HFA 100 µg = fluticasone 100 µg = budesonide 200 µg = ciclesonide 80 µg.¹³⁴⁻¹³⁶

The key variable examined statistically was the preventer-to-reliever (P : R) ratio in each of the study periods. The P : R ratio was calculated for each patient as the average beclomethasone-equivalent usage per day divided by the average salbutamol-equivalent usage per day. In accordance with other studies that have used the ratio,^{129,316-319} LABAs were not included as preventers in this ratio because they are not appropriate as single-preventer medication therapy.^{320,321} However, their efficacy should have been reflected indirectly by lowering the number of relievers required and thus increasing the P : R ratio. The ICS and SABA usages were then analysed separately to determine where any changes in the P : R ratio originated.

As SABAs are available without a prescription, and over-the-counter (OTC) supplies are not always recorded, a sensitivity analysis on SABA usage was performed. This analysis was performed on all long-term concessional patients, with the assumption that this cohort of patients received minimal supplies of non-prescription SABAs, owing to their reimbursement on the Pharmaceutical Benefits Scheme. Comparing the recorded non-prescription supplies of SABAs in the long-term concessional and non-concessional patients validated this assumption. Long-term concession patients were defined as those who received prescriptions at the concession rate throughout the entire study period.

All variables were collated and entered into a statistical software package, Statview 5.01 (Abacus Concepts Inc, Berkeley, California, US). Data were analysed statistically using the Friedman's test for overall within-group changes, and the Wilcoxon signed rank test with Bonferroni correction for post hoc assessments of significance between time periods. The Bonferroni adjusted critical value controlled for multiple comparison testing, and was obtained by dividing the original threshold P value (0.05) by the total number of comparisons made (six).^{322,323} Categorical demographic variables were compared using the Chi Square test. A significance level of $P < 0.05$ was used for the Friedman's test, and $P < 0.008$ was used for post hoc tests.^{322,323}

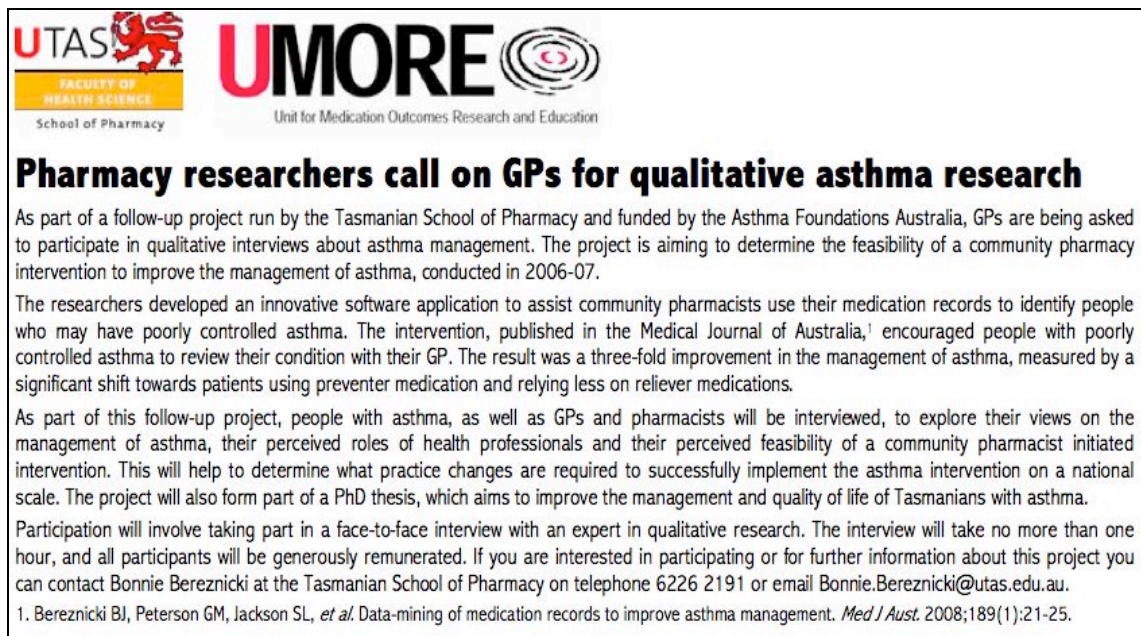
2.2.3 Qualitative component


2.2.3.1 Recruitment of participants


In order to inform local GPs about the project, a project summary was sent to the southern, northern, and north-western Divisions of General Practice in Tasmania to be included in local newsletters (Figure 15). GPs who participated in the previous intervention were sent an invitation letter (Appendix 1), project information sheet (Appendix 2) and participant consent form (Appendix 3). Community pharmacists who participated in the previous intervention were sent a letter inviting them to participate in a qualitative interview, and requesting their involvement in the recruitment of patients (Appendix 4). Pharmacists were required to fax an expression of interest form to the researchers, indicating whether they felt the study would be worthwhile and they had time to participate (Appendix 5). Pharmacists who agreed to participate in a qualitative interview were sent a pharmacist interview letter (Appendix 6), project information sheet (Appendix 2) and participant consent form (Appendix 3), and those who agreed to

assist in the recruitment of patients were sent patient recruitment instructions with the identification numbers of the former participants from their pharmacy (Appendix 7) and patient recruitment packs containing patient invitation letters (Appendix 8), project information sheets (Appendix 2) and participant consent forms (Appendix 3), as well as the required number of postage paid envelopes. Participating GPs, pharmacists and patients were offered \$200, \$100 and \$50 honoraria, respectively.

Figure 15. Excerpt a GP South (Tasmania) newsletter - February 2009



UTAS 
FACULTY OF
HEALTH SCIENCES
School of Pharmacy

UMORE 
Unit for Medication Outcomes Research and Education

Pharmacy researchers call on GPs for qualitative asthma research

As part of a follow-up project run by the Tasmanian School of Pharmacy and funded by the Asthma Foundations Australia, GPs are being asked to participate in qualitative interviews about asthma management. The project is aiming to determine the feasibility of a community pharmacy intervention to improve the management of asthma, conducted in 2006-07.

The researchers developed an innovative software application to assist community pharmacists use their medication records to identify people who may have poorly controlled asthma. The intervention, published in the Medical Journal of Australia,¹ encouraged people with poorly controlled asthma to review their condition with their GP. The result was a three-fold improvement in the management of asthma, measured by a significant shift towards patients using preventer medication and relying less on reliever medications.

As part of this follow-up project, people with asthma, as well as GPs and pharmacists will be interviewed, to explore their views on the management of asthma, their perceived roles of health professionals and their perceived feasibility of a community pharmacist initiated intervention. This will help to determine what practice changes are required to successfully implement the asthma intervention on a national scale. The project will also form part of a PhD thesis, which aims to improve the management and quality of life of Tasmanians with asthma.

Participation will involve taking part in a face-to-face interview with an expert in qualitative research. The interview will take no more than one hour, and all participants will be generously remunerated. If you are interested in participating or for further information about this project you can contact Bonnie Bereznicki at the Tasmanian School of Pharmacy on telephone 6226 2191 or email Bonnie.Bereznicki@utas.edu.au.

1. Bereznicki BJ, Peterson GM, Jackson SL, *et al*. Data-mining of medication records to improve asthma management. *Med J Aust*. 2008;189(1):21-25.

2.2.3.2 Qualitative interviews

All participants underwent a 30-40 minute semi-structured in-depth interview. The participants themselves chose the location for the interview, for example their home or workplace. The intervention process was discussed, and participants were asked to describe their views and experiences of the intervention, and any issues they felt may require attention if the intervention was to be implemented on a national scale. The face-to-face discussion guide, as displayed in Appendix 9, incorporated all of the qualitative objectives under each of the following discussion points:

- How asthma is/should be managed;
- Perceived roles of GPs and community pharmacists in the management of asthma;

- Feelings and perceptions regarding the community pharmacy asthma intervention;
- Drivers and barriers to the national implementation of a best-practice pharmacy-led asthma intervention; and
- Practice changes required to successfully implement an asthma intervention.

Different interview guides were used for patients, GPs and community pharmacists, thereby varying the content and technical complexity from the perspective of the interviewee. There was an emphasis on open questioning and exploring interesting aspects in relation to specific topics. Two researchers, trained and experienced in the interview process, independently conducted the interviews. Best practice stipulated that the interviewers were independent of the previous intervention and unknown to the participants. Care was taken to ensure that the interview procedure was consistent throughout the study period.

2.2.3.3 Handling of data

Detailed notes were taken during and after each interview, including verbatim quotes. Both interviewers who were not involved in the previous intervention participated in the analysis, to minimise any investigator bias.³²⁴ The interview notes were carefully read through several times and analysed independently by the interviewers using interpretive phenomenology. The qualitative analysis encompassed the three general phases of familiarisation, data reduction and interpretation (Table 7).

Table 7. Qualitative data analysis – interpretive phenomenology

Familiarisation	The researchers read the notes, to familiarise themselves with the data and to identify the various themes that had emerged.
Data reduction	Interview responses were analysed, identifying similarities and differences by topic and segment. All data were then summarized into key points.
Interpretation	All relevant quotes were selected for their illustrative value. Consensus was reached by discussion between the researchers. The themes were not defined in advance, and all authors agreed on the major findings that arose from the analysis.

2.2.4 Ethical approval and trial registration

The quantitative component of this project was approved by the Tasmanian Health and Medical Human Research Ethics Committee (ethics reference number H9039), and the qualitative component was approved by the Tasmanian Social Sciences Human

Research Ethics Committee (ethics reference number H10378). The study was registered with the Australian New Zealand Clinical Trial Registry (registration number ACTRN12609000196246).

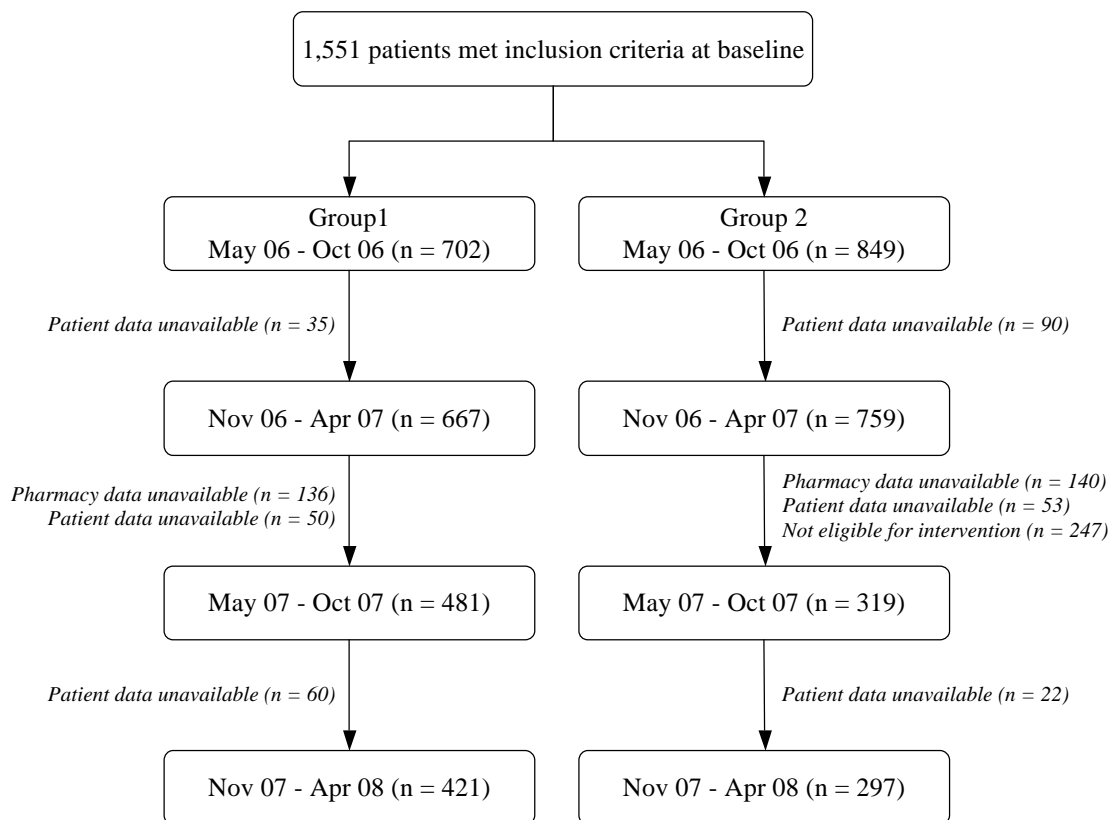
2.3 Results

2.3.1 Quantitative component

2.3.1.1 Study population

Of the 35 pharmacies that completed the original intervention, 28 (80.0%) were able to provide follow-up dispensing data. Of the seven pharmacies that were not able to provide follow-up dispensing data, three were no longer using the Fred dispensing system, and therefore had incompatible software, and four were unable to provide data due to unforeseen software issues. Figure 16 shows detailed information on the availability of patients' data in each of the time periods.

Figure 16. Number of patients' dispensing data analysed in each time period*



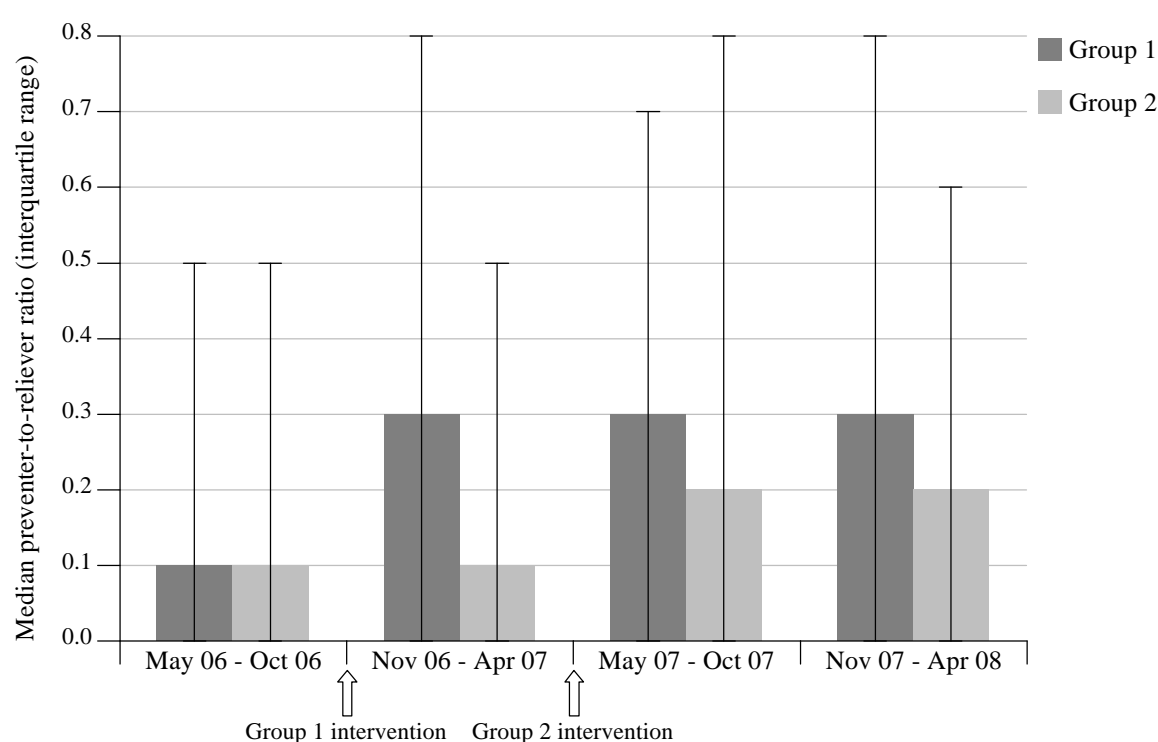
*Pharmacy data unavailable implies the patient data was unavailable due to software incompatibility or unforeseen software issues; Patient data unavailable implies the pharmacy data was available, but the patient's last prescription ever supplied by the pharmacy was dispensed prior to the data collection period; Not eligible for intervention implies the patients' data was not analysed for sustainability because they did

not receive three or more reliever canisters in the preceding six-month period and thus did not receive an intervention.

2.3.1.2 Preventer-to-reliever ratio

In Group 1, the median P : R ratio increased from 0.1 in the six-month period before the intervention, to 0.3 thereafter. In Group 2, the median P : R ratio remained at 0.1 in the first two six-month periods before the intervention, and increased to 0.2 thereafter (Figure 17).

Figure 17. Changes in preventer-to-reliever ratios over the study period



As displayed in Table 8, Friedman's test showed significant changes of the P : R ratio over time, within each group (Group 1, $\chi^2 = 12.9$, $df = 3$, $P < 0.01$; Group 2, $\chi^2 = 18.4$, $df = 3$, $P < 0.001$).

Table 8. Overall changes in P : R ratio within each group*

Patients	6-12 months pre-intervention	0-6 months pre-intervention	0-6 months post-intervention	6-12 months post-intervention	12-18 months post-intervention	P
Group 1	N/A	0.1 (0.0 - 0.5)	0.3 (0.0 - 0.8)	0.3 (0.0 - 0.7)	0.3 (0.0 - 0.8)	< 0.01
Group 2	0.1 (0.0 - 0.5)	0.1 (0.0 - 0.5)	0.2 (0.0 - 0.8)	0.2 (0.0 - 0.6)	N/A	< 0.001

*Figures represent median (interquartile range).

Table 9 displays the results of the Wilcoxon post hoc comparisons of the P : R ratio between time periods, for each group. In Group 1, post hoc comparisons showed significant increases in the P : R ratio between the 0-6 months pre-intervention period and (i) the 0-6 months post intervention period, (ii) the 6-12 months post-intervention period, and (iii) the 12-18 months post-intervention period.

In Group 2, post hoc comparisons showed significant increases in the P : R ratio between the 0-6 months pre-intervention period and (i) the 0-6 months post-intervention period, and (ii) the 6-12 months post-intervention period.

Table 9. Wilcoxon post hoc comparisons of P : R ratio within each group*

Time periods compared	Z	P
<i>Group 1</i>		
0-6 months pre-intervention to 0-6 months post-intervention	5.7	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	4.8	< 0.0001
0-6 months pre-intervention to 12-18 months post-intervention	3.7	< 0.001
0-6 months post-intervention to 6-12 months post-intervention	0.6	0.5
0-6 months post-intervention to 12-18 months post-intervention	0.2	0.8
6-12 months post-intervention to 12-18 months post-intervention	0.2	0.9
<i>Group 2</i>		
6-12 months pre-intervention to 0-6 months pre-intervention	0.7	0.5
6-12 months pre-intervention to 0-6 months post-intervention	2.6	< 0.01
6-12 months pre-intervention to 6-12 months post-intervention	1.6	0.1
0-6 months pre-intervention to 0-6 months post-intervention	4.4	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	3.7	< 0.001
0-6 months post-intervention to 6-12 months post-intervention	0.9	0.4

*Using a significance level with Bonferroni correction for multiple comparisons, $P < 0.008$.

2.3.1.3 Reliever and preventer usage

Friedman's test showed significant changes in the average daily SABA usage over time, within each group (Group 1, $\chi^2 = 282.5$, $df = 3$, $P < 0.0001$; Group 2, $\chi^2 = 178.4$, $df = 3$, $P < 0.0001$; Table 10).

Table 10. Overall changes in average daily SABA usage within each group*

Patients	6-12 months pre-intervention	0-6 months pre-intervention	0-6 months post-intervention	6-12 months post-intervention	12-18 months post-intervention	P
Group 1	N/A	655.7 (437.2 - 874.3)	425.5 (209.4 - 796.0)	437.2 (218.6 - 874.3)	218.6 (82.0 - 655.7)	< 0.0001
Group 2	655.7 (437.2 - 874.3)	437.2 (207.3 - 851.1)	655.7 (437.2 - 1092.9)	437.2 (218.6 - 874.3)	N/A	< 0.0001

*Figures represent median usage in µg (interquartile range).

Table 11 displays the results of the Wilcoxon post hoc comparisons of the daily SABA usage between time periods, for each group. In Group 1, post hoc comparisons showed significant decreases in the average daily SABA usage between the 0-6 months pre-intervention period and (i) the 0-6 months post-intervention period, (ii) the 6-12 months post-intervention period, and (iii) the 12-18 months post-intervention period. There were also significant decreases in the average daily SABA usage between the 0-6 months post-intervention and 12-18 months post-intervention periods, and between the 6-12 months post-intervention and 12-18 month post-intervention periods.

In Group 2, post hoc comparisons showed significant decreases in the average daily SABA usage between the 6-12 months pre-intervention and (i) the 0-6 months pre-intervention periods, and (ii) the 6-12 months post-intervention periods. There were also significant decreases in average daily SABA usage and between the 0-6 months post-intervention and 6-12 months post-intervention periods.

In Group 2, there were significant increases in the average daily SABA usage between the 6-12 months pre-intervention and 0-6 months post-intervention periods. There were also significant increases in the average daily SABA usage between the 0-6 months pre-intervention and (i) the 0-6 months post-intervention period, and (ii) the 6-12 months post-intervention periods.

Table 11. Wilcoxon post hoc comparisons of average daily SABA usage within each group*

Time periods compared	Z	P
<i>Group 1</i>		
0-6 months pre-intervention to 0-6 months post-intervention	14.0	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	10.8	< 0.0001
0-6 months pre-intervention to 12-18 months post-intervention	14.1	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	0.9	0.4
0-6 months post-intervention to 12-18 months post-intervention	6.8	< 0.0001
6-12 months post-intervention to 12-18 months post-intervention	7.8	< 0.0001
<i>Group 2</i>		
6-12 months pre-intervention to 0-6 months pre-intervention	11.2	< 0.0001
6-12 months pre-intervention to 0-6 months post-intervention	4.4	< 0.0001
6-12 months pre-intervention to 6-12 months post-intervention	10.4	< 0.0001
0-6 months pre-intervention to 0-6 months post-intervention	6.0	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	11.6	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	7.4	< 0.0001

*Using a significance level with Bonferroni correction for multiple comparisons, $P < 0.008$.

Table 12 displays number of SABA canisters dispensed within each group. The Friedman's test showed significant changes in the number of SABA canisters dispensed over time, within each group (Group 1, $\chi^2 = 298.0$, $df = 3$, $P < 0.0001$; Group 2, $\chi^2 = 187.2$, $df = 3$, $P < 0.0001$).

Table 12. Number of SABA canisters dispensed over the study period*

Patients	6-12 months pre-intervention	0-6 months pre-intervention	0-6 months post-intervention	6-12 months post-intervention	12-18 months post-intervention	P
Group 1	N/A	6 (4 - 8)	4 (2 - 7)	4 (2 - 8)	2 (1 - 6)	< 0.0001
Group 2	6 (2 - 8)	4 (2 - 8)	6 (4 - 10)	4 (2 - 8)	N/A	< 0.0001

*Figures represent median number of relievers (interquartile range).

Table 13 displays the results of the Wilcoxon post hoc comparisons of the number of SABA dispensed between time periods, for each group. The comparisons showed the same significant differences between time periods as the average daily SABA usage.

Table 13. Wilcoxon post hoc comparisons of SABA canisters dispensed within each group*

Time periods compared	Z	P
<i>Group 1</i>		
0-6 months pre-intervention to 0-6 months post-intervention	13.3	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	10.7	< 0.0001
0-6 months pre-intervention to 12-18 months post-intervention	14.1	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	1.0	0.3
0-6 months post-intervention to 12-18 months post-intervention	6.8	< 0.0001
6-12 months post-intervention to 12-18 months post-intervention	7.8	< 0.0001
<i>Group 2</i>		
6-12 months pre-intervention to 0-6 months pre-intervention	10.7	< 0.0001
6-12 months pre-intervention to 0-6 months post-intervention	4.3	< 0.0001
6-12 months pre-intervention to 6-12 months post-intervention	10.3	< 0.0001
0-6 months pre-intervention to 0-6 months post-intervention	6.0	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	11.4	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	7.4	< 0.0001

*Using a significance level with Bonferroni correction for multiple comparisons, $P < 0.008$.

Friedman's test showed significant changes in the average daily ICS usage over time, within each group (Group 1, $\chi^2 = 39.1$, $df = 3$, $P < 0.0001$; Group 2, $\chi^2 = 54.9$, $df = 3$, $P < 0.0001$; Table 14).

Table 14. Overall changes in average daily ICS usage within each group*

Patients	6-12 months pre-intervention	0-6 months pre-intervention	0-6 months post-intervention	6-12 months post-intervention	12-18 months post-intervention	P
Group 1	N/A	109.3 (0.0 - 327.9)	66.3 (0.0 - 315.8)	109.3 (0.0 - 327.9)	65.6 (0.0 - 303.3)	< 0.0001
Group 2	65.6 (0.0 - 327.9)	0.0 (0.0 - 271.0)	163.9 (0.0 - 409.8)	82.0 (0.0 - 327.9)	N/A	< 0.0001

*Figures represent median usage in μg (interquartile range).

Table 15 displays the results of the Wilcoxon post hoc comparisons of the daily ICS usage between time periods, for each group. In Group 1, post hoc comparisons showed significant decreases in the average daily ICS usage between the 0-6 months pre-intervention and 12-18 months post-intervention periods, between the 0-6 months post-intervention and 12-18 months post-intervention periods, and between the 6-12 months post-intervention and 12-18 months post-intervention periods.

In Group 2, post hoc comparisons showed significant decreases in the average daily ICS usage between the 6-12 months pre-intervention and 0-6 months pre-intervention periods, and between the 0-6 months post-intervention and 6-12 months post-intervention periods.

In Group 2, there were also significant increases in the average daily ICS usage between the 6-12 months pre-intervention and 6-12 months post-intervention periods, and between the 0-6 months pre-intervention and 6-12 months post-intervention periods.

Table 15. Wilcoxon post hoc comparisons of average daily ICS usage within each group*

Time periods compared	Z	P
<i>Group 1</i>		
0-6 months pre-intervention to 0-6 months post-intervention	3.1	< 0.01
0-6 months pre-intervention to 6-12 months post-intervention	1.7	0.1
0-6 months pre-intervention to 12-18 months post-intervention	4.7	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	0.7	0.5
0-6 months post-intervention to 12-18 months post-intervention	3.8	< 0.001
6-12 months post-intervention to 12-18 months post-intervention	5.5	< 0.0001
<i>Group 2</i>		
6-12 months pre-intervention to 0-6 months pre-intervention	4.5	< 0.0001
6-12 months pre-intervention to 0-6 months post-intervention	0.2	0.8
6-12 months pre-intervention to 6-12 months post-intervention	1.6	0.1
0-6 months pre-intervention to 0-6 months post-intervention	1.6	0.1
0-6 months pre-intervention to 6-12 months post-intervention	4.8	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	6.4	< 0.0001

*Using a significance level with Bonferroni correction for multiple comparisons, $P < 0.008$.

Table 16 displays the proportion of patients who received at least one supply of ICS in each six-month period. Within each group, the proportion of patients using ICS changed significantly from one period to the next. Approximately half of the patients were not using any ICS throughout most of the study period.

Table 16. Proportion of patients who received at least one supply of ICS in each period

Patients	6-12 months pre-intervention	0-6 months pre-intervention	0-6 months post-intervention	6-12 months post-intervention	12-18 months post-intervention
<i>Group 1</i>					
ICS ± LABA ± SABA	N/A	387/702 (55.1%)	347/667 (52.0%)	261/481 (54.3%)	220/421 (52.3%)
No ICS	N/A	315/702 (44.9%)	320/667 (48.0%)	220/481 (45.7%)	201/421 (47.7%)
<i>P</i> value	< 0.0001 < 0.0001 < 0.0001				
<i>Group 2</i>					
ICS ± LABA ± SABA	443/849 (52.2%)	361/759 (47.6%)	192/319 (60.2%)	167/297 (56.2%)	N/A
No ICS	406/849 (47.8%)	398/759 (52.4%)	127/319 (39.8%)	130/297 (43.8%)	N/A
<i>P</i> value	< 0.0001 < 0.0001 < 0.0001				

Table 17 clarifies the changes in ICS and SABA usage, by displaying the percent changes in median ICS and SABA average daily usage over the study period. The table displays a greater decrease in SABA usage, compared to ICS over the study period in both groups.

Table 17. Percent changes in median daily ICS and SABA usage over the study period

Time after initial data collection	ICS	SABA
<i>Group 1</i>		
6 months	−39.3%	−35.1%
12 months	0.0%	−33.3%
18 months	−40.0%	−66.6%
<i>Group 2</i>		
6 months	−100.0%	−33.3
12 months	149.8%	0.0%
18 months	25.0%	−33.3%
Average percent change over the study period	−0.75%	−33.6%

2.3.1.4 Sensitivity analysis

A significantly reduced proportion of long-term concessional patients collected one or more recorded supply of non-prescription SABA, as compared to the non-concessional

patients (31/519 [6.0%] versus 159/1032 [15.4%] respectively, $\chi^2 = 28.6$, $P < 0.0001$). Friedman's test showed significant decreases in the average daily SABA usage over time, within each group (Group 1, $\chi^2 = 282.5$, $df = 3$, $P < 0.0001$; Group 2, $\chi^2 = 178.4$, $df = 3$, $P < 0.0001$; Table 18).

Table 18. Overall changes in average daily SABA usage amongst long-term concessional patients*

Patients	6-12 months pre-intervention	0-6 months pre-intervention	0-6 months post-intervention	6-12 months post-intervention	12-18 months post-intervention	P
Group 1	N/A	655.7 (437.2 - 874.3)	439.6 (216.2 - 829.0)	437.2 (218.6 - 874.3)	273.2 (0.0 - 655.7)	< 0.0001
Group 2	874.3 (437.2 - 1120.2)	800.0 (594.8 - 1098.9)	655.7 (437.2 - 1092.9)	437.2 (218.6 - 874.3)	N/A	< 0.0001

*Figures represent median (interquartile range).

Table 19 displays the results of the Wilcoxon post hoc comparisons of the daily SABA usage between time periods, for long-term concessional patients in each group. The post hoc analyses confirmed the significant decrease in SABA usage after each intervention.

Table 19. Wilcoxon post hoc comparisons of SABA usage amongst long-term concessional patients*

Time periods compared	Z	P
<i>Group 1</i>		
0-6 months pre-intervention to 0-6 months post-intervention	9.7	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	7.4	< 0.0001
0-6 months pre-intervention to 12-18 months post-intervention	12.3	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	1.9	< 0.1
0-6 months post-intervention to 12-18 months post-intervention	5.4	< 0.0001
6-12 months post-intervention to 12-18 months post-intervention	7.5	< 0.0001
<i>Group 2</i>		
6-12 months pre-intervention to 0-6 months pre-intervention	0.2	0.9
6-12 months pre-intervention to 0-6 months post-intervention	3.2	< 0.01
6-12 months pre-intervention to 6-12 months post-intervention	9.2	< 0.0001
0-6 months pre-intervention to 0-6 months post-intervention	4.0	< 0.0001
0-6 months pre-intervention to 6-12 months post-intervention	10.0	< 0.0001
0-6 months post-intervention to 6-12 months post-intervention	6.6	< 0.0001

*Using a significance level with Bonferroni correction for multiple comparisons, $P < 0.008$.

2.3.2 Qualitative component

2.3.2.1 Study population

Of the 26 GPs, 24 pharmacists, and 81 patients who were invited to participate, six (23.1%), 10 (41.7%), and 10 (12.3%) were enrolled in the study, respectively. One female and five male GPs were interviewed. They were aged between 44 and 56 years, had an average of 26 years experience in general practice, and worked 25-50 hours per week. Three female and seven male community pharmacists were interviewed. They were aged between 31 and 55 years, had an average of 18 years experience in community pharmacy, and worked 30-60 hours per week. Seven female and three male patients, aged between 51 and 96 years, were interviewed. Typically, they visited their GP specifically for an asthma consultation once or twice a year, or more often if they had other co-morbidities. However, several reported actively avoiding asthma-related medical consultations by telephoning their GP to obtain repeat prescriptions. Only one patient had seen a respiratory specialist in the previous 12 months, and most had never seen a specialist. One had been hospitalised for asthma on five occasions. Table 20 displays the sample of GPs, community pharmacist and patients who participated in an interview.

Table 20. Number of participants interviewed

Respondent type	Location		Total
	North-western Tasmania	Southern Tasmania	
General practitioners	4	2	6
Pharmacists	6	4	10
Patients with asthma	4	6	10
Total	14	12	26

2.3.2.2 General practitioners

Table 21 displays the relevant demographical profiles of each GP interviewed.

Table 21. General practitioners' profiles

Gender	Age	Years in general practice	Hours practice per week	Number patients in total practice	Estimated percentage of patients with asthma in practice
Male	45	20	50	Unknown	≈10%
Male	49	25	45	15,000	≈10%
Male	55	30	50	20,000	≈5%
Male	53	28	45	11,000	≈5%
Female	56	31	25	Unknown	5-10%
Male	44	20	40+	Unknown	8%

Most GPs believed that community pharmacists were well placed to refer patients to GPs when they had underestimated the severity of their asthma and were over-relying on reliever medications. The intervention was perceived as an extension of pharmacists' responsibilities:

“It was an excellent process as I can prescribe six months of Ventolin[®] and six months of Seretide[®] and they may stop the Seretide[®] and just use the Ventolin[®] and I don't have any way to check up on this [but pharmacists do].” (Male, 49)

“Pharmacists are good monitors of over users of prescriptions.”
(Male, 53)

“They [pharmacists] can identify if there is too much Ventolin[®] being used.” (Male, 55)

“Pharmacists can be an early warning system.” (Male, 44)

The positive views of the intervention were dependent on good GP/pharmacist relationships:

“Pharmacists are a good point of advice especially if there is too much Ventolin[®] used, and I don't mean a fly-by-nighter. It is more when you have a pharmacist where you have a good relationship.” (Male, 49)

There was also some apprehension towards the intervention process. Any negative views of the intervention seemed to be related to a lack of understanding or a reluctance

to accept pharmacist input, especially if they perceived this as an encroachment on their own area of responsibility:

“As long as they [pharmacists] don’t overstep their mark.”
(Male, 49)

Some GPs questioned the credibility of pharmacists, and raised a potential conflict of interest in promoting good asthma management in a retail environment:

“...Because they [pharmacists] sell stuff... that’s their business...
there’s always going to be a conflict of interest.” (Male GP, 53)

General practitioners would welcome advice from pharmacists at the time of interventions, so they could make notes to raise the issue with patients at subsequent visits. An area where GPs believed the intervention could have been improved was the lack of direct communication provided to them about their patients. They felt that they should have been informed that their patients were given intervention packs:

“If they [pharmacists] suggest something to my patients then I expect to be told... The patient could get confused if the GP is not aware of what has been said to them by the pharmacist.”
(Male, 55)

There were suggestions made to inform GPs at the time of the intervention:

“If there was patient consent the pharmacist and doctor could discuss it, or even better the pharmacy software could send a message electronically... like a pathology report.” (Male, 45)

General practitioners expressed that patients were rarely forthcoming about problems with their asthma, even after being referred for an asthma management review by their pharmacists. One aspect commented on, was that the intervention relied on patients to initiate contact with their GP, and further when they did go to the GP, to inform the GP what they had been given and told:

“Often patients come and don’t say anything. It would be helpful if they would say that my pharmacist said I had to come and see you.” (Male, 45)

A related issue was that it was hard to reach chronically non-adherent asthma patients. Even if presented with an intervention pack, it was thought to be unlikely that such patients would take any action. They believed that this issue might have decreased the efficiency of the intervention process:

“It’s always going to be tough to get to the noncompliant.”

(Male, 55)

2.3.2.3 Community pharmacists

Table 22 displays the relevant demographical profiles of each community pharmacist interviewed.

Table 22. Community pharmacists’ profiles

Gender	Age	Owner or manager	Years in community pharmacy	Hours practice per week	Accredited to do HMR*
Male	40	Owner	18	60	No
Male	37	Owner	14	50	No
Male	31	Owner	9	48	No
Male	32	Manager	9	43	No
Female	34	Owner	11	38	Yes
Female	41	Owner	18	25	Yes
Male	50	Owner	28	60	Yes
Male	44	Owner	20	50	No
Male	50	Owner	27	30-35	No
Female	55	Owner	30	30	No

*Home Medication Review

Pharmacists felt that patients can be apathetic about asthma, fail to seek medical advice and can self-medicate with their own or other people’s reliever medication. The perception seemed to be that the use of asthma relievers has been ‘normalised in the community’:

“They [patients] can use a puffer every few days and when you talk to them they think they are well off.” (Male, 37)

“Most [patients] have a fix it now mentality rather than use a preventer.” (Female, 34)

Pharmacists assessed the asthma intervention positively. They spoke of being more engaged in asthma-related discussions with patients following the intervention and believed that a larger roll-out of the asthma intervention would be a positive move towards recognition of their role in patient care:

“It jogged the memory about what we should be doing with asthma... we can be a lot more proactive.” (Female, 41)

“We had some good results... one particularly resistant patient went to the GP and now takes a preventer.” (Male, 44)

“I’d hope that all pharmacists would want to be involved... It’s what we’re trained for...” (Female, 34)

The use of dispensing data to identify patients who may have suboptimal management of their asthma was seen to be a positive, as there was a lot of information retained by pharmacists, which could be used to benefit patients:

“We have a lot of information in our computers which we don’t use.” (Male, 40)

The data mining software program was positively assessed as easy to use and the intervention was implemented very easily, with minimal disruptions to workflow:

“The time taken was minimal and it was not imposing.”
(Male, 32)

“The system was easy to use - we figured out how to use it.”
(Male, 31)

“It did not take any time at all. It was a breeze compared to [another research project] where everything had to be done on paper... It [this project] was all electronic so it was easy.”
(Male, 40)

There were some suggestions made for an improvement in the intervention process, including more direct involvement of the GP. Like GPs, pharmacists suggested that it would be better if GPs were informed at the same time as patients perhaps with a courtesy letter or electronic notification:

“It would have been good to talk to the doctor, but I don’t know about privacy.” (Male, 37)

“It’s in the pharmacist’s best interest for the GP to be informed.”
(Male, 31)

2.3.2.4 Patients with asthma

Table 23 displays the relevant demographical profiles of each patient interviewed.

Table 23. Patients’ profiles

Gender	Age	Visits to GP for asthma in last 12 months	Visit to respiratory specialist in last 12 months	Ever hospitalised for asthma
Male	67	2-3	No	No
Female	62	1-2	No	No
Female	96	12-20	No	No
Male	55	1-2	No	No
Female	56	1-2	No	No
Female	84	12	Yes	No
Female	55	1	No	Yes
Female	51	0	No	No
Male	70	1-2	No	No
Female	64	3-4	No	No

Patients spoke of their pharmacist as a good person and reported a strong personal relationship. Frequently, it was this relationship that was important to patients’ acceptance of any increased pharmacy activity:

“He [the pharmacist] always asks about me and how I am going, and he has given me some helpful advice on my asthma.”
(Male, 67)

“Pharmacists are good as [you can ask a question and] they don’t make you feel like a goose.” (Female, 62)

“I see him [the pharmacist] more than the doctor. He tells me what to do, what the medications are all for, he’s really helpful.”
(Male, 70)

However, it was evident that patients' expectations of pharmacists' activity were relatively low, and they more commonly asked their doctor for advice on their asthma:

"If I needed some advice I'd go to the doctors." (Female, 64)

"She is the doctor so she should be the one telling me [about asthma management]." (Male 67)

Most patients perceived their asthma as currently well managed and controlled. However, these perceptions were in direct contrast to both the evidence they provided of the amount of reliever medication required daily and the symptoms they described:

"I am always short of breath... some people have bad asthma, but that is not me..." (Female, 84)

"I measure my asthma by my shortness of breath which is always present." (Male, 67)

"I have the Flixotide[®] in the morning and at night and have one or two puffs of Ventolin[®] every four hours." (Female, 55)

Patients, especially those who had good relationships with their local pharmacist, were very accepting of the asthma intervention and the subsequent mailed out information, and they were pleased someone was keeping track of their health:

"Anything they can do to improve how asthma is treated is OK by me." (Female, 55)

"It's good that someone's looking into it [asthma]." (Female, 51)

Most patients interviewed did not take any action as a result of the intervention to either visit their doctor to discuss their asthma or to change their asthma therapy. Most had the opinion that their asthma was well controlled and did not see the need to visit their GP:

"I didn't see my doctor as I felt alright, and I didn't mention anything to him." (Male, 67)

"If I was feeling poorly then I would have done something." (Female, 84)

“I didn’t follow up because nothing could be changed anyway...” (Female, 55)

Some perceived their GPs as busy people, so they did not want to bother their GP with something that was not really an issue in their minds:

“I wonder if it is worthwhile [contacting her GP] as I don’t want to be a nuisance.” (Female, 84)

“I know they [GPs] are busy, and I don’t want to take up too much of their time. I would have to have a hand cut off to worry them.” (Female, 62)

Thus, patients were reluctant to adopt suggestions from pharmacists to make GP appointments for asthma reviews, or when they did make an appointment, they may not have raised any issues with their asthma.

2.4 Discussion

2.4.1 Quantitative component

This project demonstrated a sustained improvement in the P : R ratio for at least 12 months after the intervention. It has been shown that the P : R ratio can be applied as a surrogate measure to assess the quality of prescribing for asthma, and is an important factor related to asthma morbidity.^{129,318} An increased P : R ratio has been associated with improved asthma symptoms,³¹⁸ reduced need for rescue courses of oral prednisolone,¹²⁹ and reduced emergency department visits,³¹⁶ hospital admissions³¹⁹ and urgent GP visits.³¹⁷

There has been other studies examining asthma management which have used the number of canisters^{130,131} or defined daily doses^{129,319} as a measure of ICS use. The limitation of using the number of canisters is that it does not account for the number of doses per canister or differing drug potencies, whereas a limitation of using defined daily doses is the poor representation of the widely accepted dose equivalence. A particular strength of this study is the fact that the potencies and doses per canister were taken into account, allowing a more accurate representation of ICS and SABA use, and therefore ensuring an accurate P : R ratio.

It has previously been demonstrated that dispensing of medium-to-high level ICS therapy is associated with a reduced risk of ICU admission, whereas high level inhaled SABA dispensing is associated with an increased risk of both ICU admission and endotracheal intubation for asthma.¹³¹ Importantly, stratified analysis indicated that this excess risk is observed only among patients not receiving ICS therapy.¹³¹ Therefore, the increased P : R ratio reported by this project should be interpreted with caution. Despite the fact that the P : R ratio was the primary outcome measure used in this project, further analyses were necessary in order to determine whether the increase in the P : R ratio resulted from an increased preventer usage or a decreased reliever usage, before any conclusions could be drawn.

Further analysis found that the increased P : R ratio was largely due to a reduction in the average daily use of reliever medication. A number of international studies have demonstrated improved asthma outcomes with decreased reliance on reliever medications.³²⁵⁻³²⁷

The average salbutamol-equivalent daily usages of SABA ranged from 218.6 µg to 655.7 µg, which is equivalent to 2-6 puffs per day, over the study period. Unfortunately, this range of daily SABA consumption is well above what is recommended by the NAC and Asthma Foundations Australia, who state that usage of reliever medication on three or more occasions per week is indicative of suboptimal asthma control.^{59,328} According to Australian asthma management guidelines, and assuming all dispensed medication had been consumed, patients using this quantity of reliever medication should be classed as having poor asthma control, and should be receiving regular ICS therapy.⁵⁹ The assumption that dispensing correlates with medication use was a limitation of this study, as discussed later.

While it was encouraging to see a sustained improvement in the P : R ratio and decrease in reliever usage, it was somewhat disappointing that the usage of ICS did not increase over the study period. The median beclomethasone-HFA equivalent daily usage of ICS over the study period fell within or below the 'low dose' range according to the NAC.⁵⁹ Assuming all dispensed medication had been consumed, the average daily usage of SABA reported over the study period indicated that the majority of patients analysed would be classified as having poor asthma control, and should therefore be maintained

on moderate-to-high dosages of ICS, as well as a LABA.⁵⁹ Unfortunately, approximately half of the patients were not using any ICS over the study period.

Inadequate use of ICS could be due to under-prescribing and/or poor adherence with therapy. It has been found that a large proportion of patients with asthma do not understand the role of their medications and have many misconceptions and fears in regard to ICS, reducing their willingness to use them.²⁶³ In addition, it has been widely demonstrated that patients prefer to manage their asthma as an acute intermittent disorder rather than a chronic ongoing disease that needs monitoring and managing.⁷⁵⁻⁷⁷ Patients' perceptions of their condition and their need for treatment limit the adherence to ICS therapy, and therefore the reported effectiveness of ICS. Barriers to ICS use must be overcome before widespread benefits of ICS therapy are seen.

The results showed decreases in reliever usage after the intervention in Group 1, but increases in reliever usage after the intervention amongst patients in Group 2. Furthermore, the preventer usage decreased immediately after the intervention in Group 1, but increased immediately after the intervention in Group 2. While these patterns in reliever and preventer usage resulted in increases in the P : R ratios in both groups, it is important to note the effect of seasonal variation on the results. Group 1 received the intervention in late October 2006, whereas Group 2 received the intervention in late April 2007. Therefore, warmer summer months were represented in Group 1's 0-6 month post-intervention dispensing data, and colder winter months were represented in Group 2's 0-6 month post-intervention data. Winter months often result in poor asthma control,^{329,330} which may explain the differences in preventer usage from one six-month period to the next.

There are potential limitations to the quantitative component of this study. It was assumed that the dispensed quantity of reliever medication equated with actual medication consumption, but factors such as storing relievers in different sites, sharing medication with family members and misplacing medication could complicate the picture. It is also possible that non-prescription supply of relievers, which is not always recorded in the dispensing software, resulted in underestimation of reliever medication usage. Underestimation may also have arisen from the assumption that asthma medications were not being dispensed at other pharmacies. However, the same level of underestimation would have applied to both groups and in all study periods.

Furthermore, the research team attempted to account for this underestimation in the patient identification algorithm used by the data mining software, by being considerably generous in the quantity of relievers that indicated suboptimal management.

Not all of the patients originally included in the study were eligible for inclusion in the follow-up study. Ineligible patients either did not receive the intervention, or did not have available data at the time of follow-up. It could not be assumed that the unavailability of patient data implied that the patient was no longer using asthma medication. Thus, it was deemed more accurate to exclude these patients, avoiding skewing of the data. However, when interpreting the results presented here it should be borne in mind that the outcomes only apply to half of the patients in the original sample. Furthermore, all data were collected in one single state (Tasmania), therefore caution must be exercised in extrapolating the findings to the rest of the Australian population as there may be local effects not present in other Australian states or territories.

2.4.2 Qualitative component

This study provided valuable information regarding the perceptions of GPs, community pharmacists and patients towards a community pharmacy-based asthma intervention. The acceptance and support of these key stakeholders is vital to ensure adequate uptake and effectiveness of future interventions. Although there have been a number of community pharmacy-based asthma interventions published which report improved patient outcomes,^{301,303,331,332} this seems to be the first data reported on the views of GPs, pharmacists, and patients of such an intervention.

There was a general acceptance of the intervention process by participants. Both GPs and patients expected pharmacists to intervene when patients' therapies could be suboptimal or detrimental to their health. Indeed, the patients were very accepting of the intervention as it provided both positive attention and reassurance that their medications were being actively monitored.

The acceptance by GPs of pharmacy interventions seemed dependent on the existing relationships with pharmacists. If the relationship was professionally cordial and respectful then any information provided to GPs was generally well received. GPs were sometimes reluctant to accept pharmacist input resulting from interventions if they perceived this as an encroachment on their own area of responsibility. This finding is in

line with previous studies, which have shown that GPs tend to express concerns about pharmacists assuming roles they considered to be general practice activities.³³³⁻³³⁵ It has previously been reported that GPs may sometimes be offended by the introduction of a pharmacist-led health service, feeling that it implied shortcomings in their existing level of care.³³⁶ This means that pharmacists need to ensure that perceived boundaries in patient care are approached with caution in order to reduce the risk of misinterpretation about the intent of these types of interventions. Another concern was the credibility of pharmacists, and the potential conflict of interest of promoting health in a retail environment. Previous studies have demonstrated that many GPs see community pharmacists as business-people, shopkeepers or specialist retailers, and believe that this represents a conflict of interest in healthcare.^{333,337,338} Interestingly, a previous study of patients' perceptions suggested that this conflict may, in practice, not be overly significant; many of the participants were able to recall experiences of their own where a pharmacist had clearly put patients before profit, not just in respect of their health, but also in terms of convenience and financial gain for the patient.³³⁹

GPs would welcome advice from pharmacists at the time of interventions, so they could make notes to raise the issue with patients at subsequent visits. With this change to the procedure, it is likely that the number of asthma reviews would increase, as the onus on the patient to initiate action would be reduced. The researchers discouraged this initial pharmacist/GP contact in the original intervention due to concerns about privacy and patient consent. If direct notification of GPs is to be used at the time of asthma interventions then there will be a need to advise GPs easily and efficiently, and patient consent in this process needs to be taken into account. This could involve some form of electronic notification, as GPs, in most cases, would not want to receive a phone call from pharmacists given the perceived non-urgency of the review. Thus, a business practice change may be required to accommodate electronic communication with GPs by pharmacists.

Pharmacists believed that a national roll-out of the asthma intervention would be a positive move towards improved asthma management in the community. It was encouraging to learn that community pharmacists implemented the intervention very easily, with minimal disruptions to workflow. Time has clearly been identified in previous studies as a major factor that significantly prevents community pharmacists from undertaking any additional extended role in healthcare.^{11-14,340,341} The workload in

community practice is such that research is perceived as having a low priority because it would have to be taken on as an additional role.¹³ Academic researchers should be sensitive to time constraints and responsibilities of community-based investigators when they develop study procedures. If community pharmacists are to become involved in pharmacy practice research, it is necessary to develop a strategy that recognises the workload issues in community pharmacy practice.

Patients' general satisfaction with pharmacy services was high, but their perceived benefit of the intervention was lower. This is in line with previous results from satisfaction studies, confirming satisfaction ratings with pharmacy services are generally high, although patients' expectations of pharmacists' capabilities are low.^{338,342-345} It is apparent that patients expect their pharmacist to process prescriptions rapidly and provide basic medication information, and that pharmacists are effective in meeting these expectations. However, most consumers apparently do not expect to consult with their pharmacist or receive pharmaceutical care services.³⁴³ These comments convey the important message that much work still needs to be done to educate the public about the training and roles of the pharmacist.³⁴³ Unfortunately, the public's poor knowledge and low expectations can justify a reduced desire for an extended role of the pharmacist in the community.³⁴²

Patients were reluctant to adopt suggestions from pharmacists to make GP appointments for asthma reviews, or when they did make an appointment, they may not have raised any issues with their asthma. While there is an appreciation of pharmacists' interest in patient health, this did not necessarily translate into compliance with the suggestions made at the time of the intervention. The reason for this related primarily to patients' optimistic views of their asthma control. All patients seemed to accept they would have asthma symptoms throughout their life, and they did not expect that an improvement in their asthma management was possible. This is in keeping with the substantial evidence that patients with asthma tend to under-estimate their asthma severity,^{46,51,52,55,281,282} and it represents a major barrier to the uptake of asthma interventions. It was interesting that despite these perceptions and reluctance to comply with the suggestions made at the time of the intervention, patients were pleased that 'something was being done' to help patients with asthma. This suggests that patients may be failing to recognise their own role in managing their asthma, and more education may be required to encourage patients to take a more proactive approach with their asthma management. Furthermore,

patients need to be made aware that putting up with their symptoms may actually be detrimental to their health,¹⁸ and that complete control of asthma is achievable in the majority of patients.²⁷

It is possible that patients' under-estimation of their symptom severity may have influenced the reported success of the intervention, as patients who considered their asthma as well controlled were unlikely to have sought further medical advice. Most interviewed patients assumed their asthma was well controlled because any symptoms were alleviated with relievers, and they did not want to 'bother' their busy GPs. This means that few GP appointments were made and even fewer asthma discussions ensued, thus reducing the beneficial outcomes of the program. Despite this low number, the quantitative data indicated a three-fold increase in the preventer-to-reliever ratio after the intervention.⁵ Clearly those patients who did attend the GP for medication review had a positive outcome in terms of improved preventer usage and a decreased reliance on reliever medication. It also suggests that the educational material provided by the pharmacist may have had some impact on asthma management. The positive outcome when patients were reviewed by the GP underscores the importance of the review process. Nevertheless, the main limitation to the uptake and effectiveness of asthma interventions may be patients' views and acceptance of their asthma symptoms. More research may be required to further explore patients' beliefs and perceptions about asthma in order to determine the best way to target health behaviours amenable to an intervention.

There are limitations to the qualitative component of this study. Whereas a large number of GPs, pharmacists and patients with asthma were approached, many failed to respond to the request for their involvement or stated that they were unable to participate. The absence of these opinions may have resulted in biases within the data. It should also be noted that the respondent sample is inherently biased for two reasons. Firstly, these participants had already demonstrated willingness to participate in such research. Secondly, the interviews were administered after participants learned of the positive results of the intervention. Furthermore, the study was conducted by selecting a sample of respondents from northern and southern Tasmania. Thus, the findings may not be representative of the total Australian experience of the management of patients with asthma. As in all qualitative studies, the generalisability of the results is conceptual rather than statistical.³⁴⁶ However, qualitative studies are applicable for exploratory

work even though they are unable to test hypotheses and are not automatically generalisable. To explore the extent and prevalence of views expressed a quantitative approach is needed. However, the findings may be generalised as the attitudes expressed here have been reported elsewhere for patients, GPs and pharmacists.^{11-14,333-345} Nevertheless, the results provide valuable information regarding the perceived feasibility of a community pharmacy-based asthma intervention. It allowed for exploration of participants' views and experiences of the intervention, and the findings provide impetus for future research in this area.

2.5 Conclusions

This study reinforces the concept that community pharmacists are ideally placed to screen for patients who may have suboptimal asthma control, with the potential to address critical issues in asthma management in the community. The intervention described required minimal time and training on the part of the pharmacist,⁵ yet resulted in significant, sustained improvements in the ratio of dispensed preventer medications to reliever medications.

The qualitative component of this project indicated that there is room for improvement in the efficiency of the asthma intervention so that more patients identified with potentially sub-optimally managed asthma could be reviewed by GPs. The result of more efficient asthma interventions would flow through to an even greater success rate in terms of preventer usage.

In conclusion, a national roll-out of the asthma intervention, with an improved process for targeting patients and involving GPs, should be feasible and well accepted. To gain sustained improvements in asthma management, the intervention should be repeated at least once every 12 months. The intervention has the potential to show widespread improvements in asthma management, resulting in better asthma control and improved health outcomes for Australia.

CHAPTER THREE:

UPTAKE AND EFFECTIVENESS OF A COMMUNITY PHARMACY INTERVENTION TO IMPROVE THE MANAGEMENT OF ASTHMA

3.1 Aim and objectives

This study aimed to utilise community pharmacy dispensing records to test the uptake and effectiveness of two different types of community pharmacy-based asthma interventions across three Australian states. Specifically, the objectives were to:

- Determine how the uptake by pharmacists influences the effectiveness of mailed and face-to-face asthma interventions;
- Significantly improve the preventer-to-reliever asthma medication ratio in the intervention cohort compared to control;
- Significantly improve the patient-reported asthma control, asthma-related quality of life and medication adherence in the intervention cohort compared to control; and
- Determine the perceptions of pharmacists, GPs and patients towards the intervention program.

3.2 Methods

3.2.1 Study design and setting

This study was a community pharmacy-based intervention, designed to improve the management of asthma. The study involved the modification of a software application so that pharmacists could use it to identify patients whose asthma may not be well managed, as evidenced by a high provision of reliever medications. This was a multicentre study, involving three Australian universities in Tasmania, Victoria and South Australia. Researchers at the University of Tasmania managed the study and oversaw the intervention in Tasmanian pharmacies, while researchers at Monash University and the University of South Australia oversaw the intervention in Victorian and South Australian pharmacies, respectively.

3.2.2 The data mining software

In 2006, researchers at the Tasmanian School of Pharmacy developed a data mining software application ('MedeMine') that seamlessly extracts data from the market-leading pharmacy dispensing software system in Australia (Fred Dispense; Fred Health). About 50% of community pharmacies in Australia use this dispensing system.

The information technology development under this study involved modifying the existing software application to identify patients with poorly managed asthma, as evidenced by the quantity of inhaled reliever medication dispensed in the preceding 12 months. Using a pre-specified algorithm, the program identified patients who had received six or more relievers (inhaled SABAs) in the preceding 12 months. This indicated that they may have been using, on average, three or more doses per day of reliever medication, which exceeds the level recommended in current guidelines for optimal asthma control.⁵⁹ To ensure that patients who were likely to be consistent (rather than seasonal) high users of reliever medication were identified, eligible patients needed to have received at least three SABA canisters in each of the two preceding six-month periods.

Patients receiving regular preventer medications (ICS) were also identified if they fulfilled the aforementioned criteria, as they may have been receiving a dose of ICS that was too low or may have been using their ICS incorrectly. In either case, they may have needed a review of their asthma therapy.

Specific exclusions were written into the program algorithm to ensure that the patients selected for our study were likely to be people with poorly managed asthma who were under the care of a GP. The program excluded patients receiving:

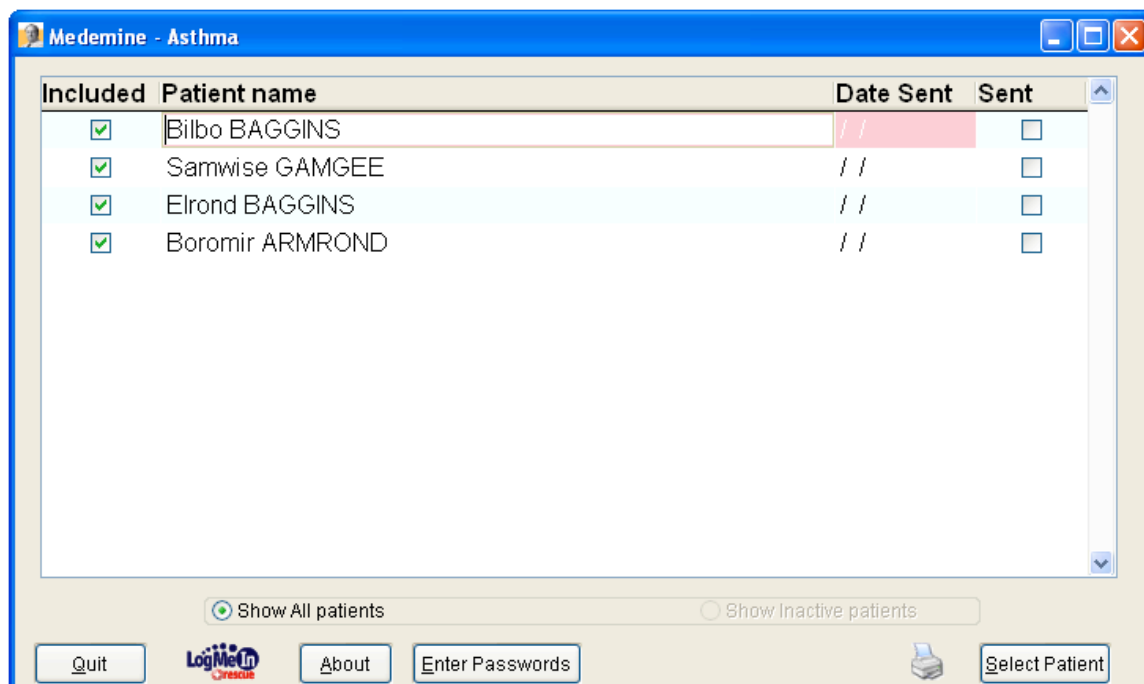
- Inhaled anticholinergics (tiotropium or ipratropium) or oral methylxanthines (theophylline or choline theophyllinate), indicating the likely presence of chronic obstructive pulmonary disease (COPD); or
- Leukotriene-receptor antagonists (montelukast or zafirlukast), indicating that the patient may either be under 18 years of age, or an adult with the probable presence of severe asthma, meaning the patient was likely to be under the care of a respiratory specialist.

The data mining program automatically ranked the list of identified patients in order of greatest to least number of reliever canisters dispensed in the preceding 12 months. The patient receiving the greatest number of relievers was randomly assigned to the intervention or control group, with subsequent patients being alternately assigned to the control or intervention group. For each patient assigned to the control group, two patients were assigned to the intervention group. This ensured an approximately even distribution of patients across the mailed intervention group, the face-to-face-intervention group and the control group.

The initial exclusion and group allocation process was concealed from the pharmacist and occurred automatically upon running the application ('MedeMine-for-Asthma'), with only the resulting list of intervention patients available for viewing. To ensure an even geographical spread of intervention and control patients, the allocation process was repeated in each pharmacy.

Figure 18 displays a screen shot of an example list of patients identified using MedeMine-for-Asthma. Personalised letters, coded surveys and address labels could also be printed from this screen.

Figure 18. List of identified patients in MedeMine-for-Asthma



A patient's dispensing information could be viewed in detail by highlighting the patient's name and clicking on 'select patient.' Dispensing information on the

MedeMine-for-Asthma screen, as shown in Figure 19, was engineered to look the same as that seen in the Fred dispensing system so that pharmacists would have an instant familiarity with the layout and presentation of the information. The patient screen used four tabs ('asthma-related dispensings,' 'collated history,' 'all dispensing history' and 'extra information'). The first three tabs displayed the patient's history in different ways; the 'asthma-related dispensings' tab showed details of all respiratory medication, the 'collated history' counted the number of supplies of each medication dispensed, and 'all dispensing history' displayed a sequential history for the patient. How much information was displayed was determined by selecting 'months history to display' (1, 3, 6, 9, 12 or all). The 'extra information' tab gave the pharmacist the facility to enter free text relating to the patient. Patients could be excluded from the study by selecting a reason from the drop-down 'reason for exclusion' menu on the top right-hand side of the screen.

Figure 19. Viewing patient dispensing history in MedeMine-for-Asthma

The screenshot shows the 'Viewing Asthma trial for Bilbo BAGGINS' window. It includes a patient information box, a 'Reason for Exclusion' dropdown, and fields for 'Initial Letter Printed on' and 'Second Letter Printed on'. Below these are radio buttons for 'Months History to display' (1, 3, 6, 9, 12, All), with '12' selected. The main area contains four tabs: 'Asthma-related Dispensings' (selected), 'Collated History', 'All Dispensing History', and 'Extra Information'. The 'Asthma-related Dispensings' tab displays a table of dispensing records.

Disp	Drug Name	Qty	Directions	Doc	Rpt	Dp	\$	By
23/04	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	3	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8883
27/03	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	2	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8881
28/02	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	1	6.50	NB
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8879
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU					8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	50mcg 60d		mouth TWICE a day **REGU					8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-AERO 200 Dose		TWO puffs by mouth every					8873
28/11	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	4	6.40	DC

At the bottom of the window are 'Close' and 'Print Letters' buttons.

3.2.3 Sample size

Based on sample size calculations using the normal approximation to the binomial distribution and incorporating a continuity correction, a total of 788 patients was estimated as being statistically adequate at a power of 80% and $P = 0.05$. This was

based on the assumption that the intervention would result in an average 0.2 difference in the preventer-to-reliever ratios, as demonstrated in a previous pharmacy-based asthma intervention.⁵

3.2.4 Pharmacy recruitment

A convenience sample of community pharmacies throughout Tasmania, Victoria and South Australia were informed about the study via telephone, and sent a letter (Appendix 10) and project synopsis (Appendix 11) informing them about the study and inviting them to participate if they were a current user of the Fred dispensing system. The intention was to recruit at least 60 pharmacies. In Tasmania, many pharmacies that were known to use the Fred dispensing system were not invited to participate. This was due to their prior participation in the pilot study,^{5,304} and the possibility that the inclusion of these pharmacies may have skewed the pre-intervention data. In Victoria and South Australia, there was no prior knowledge of which pharmacies did and did not use the Fred dispensing system. Thus, pharmacies were contacted until recruitment targets were reached.

Pharmacists were required to fax an expression of interest form to the researchers, indicating whether they felt the study would be worthwhile and they had time to participate (Appendix 12). Follow-up phone calls were made to pharmacists who did not send back the expression of interest form.

Information and education sessions were held in each state for pharmacists involved in the study. For those pharmacists unable to attend an information session, a personalised one-on-one visit was arranged closer to the time of the project implementation. The information sessions were two hours in length and covered an overview of asthma management in Australia, an outline of the study's aim and methods, and a demonstration of the MedeMine-for-Asthma software. In addition, a respiratory specialist physician from each region attended the information sessions and discussed the incidence and morbidities of asthma and current management guidelines.


Each pharmacy was remunerated for their time attending the information sessions and for their involvement in the study. A nominal payment of \$200 per pharmacy, plus reimbursement for the postage costs incurred throughout the course of the study, was made in two instalments, after the intervention period and at the study's completion.

The MedeMine-for-Asthma program calculated the amount that could be invoiced based on the number of patient letters that had been mailed.

3.2.5 Dissemination of project information to GPs

To provide advanced warning to local GPs in each region, information was sent to the relevant Divisions of General Practice in each state, to be published in a monthly newsletter (Figure 20). In addition, pharmacists were provided with a GP information sheet (Appendix 13) to send to local GPs.

Figure 20. Excerpt a GP North (Tasmania) newsletter - June 2008



Asthma Patient Education Project

Community pharmacists assisting GPs identify patients with suboptimal control of asthma

As part of a project run by the Tasmanian School of Pharmacy and funded by the Department of Health and Ageing as part of the 4th Community Pharmacy Agreement, patients who have suboptimal asthma control will be targeted for a review. The Unit for Medication Outcomes Research and Education (UMORE) has developed a software program, which enables pharmacists to identify patients with asthma whose control may be suboptimal.

Utilising dispensing records, patients who have six or more reliever medications dispensed in the preceding 12 months, potentially indicating suboptimal control, will be identified. Assuming the patient has utilised all of the reliever medication in the preceding 12 months, this equates to at least daily use of a reliever medication. The researchers, using the National Asthma Council guidelines, specify that use of a reliever medication more than three times per week indicates suboptimal control. Patients who are likely to have chronic obstructive pulmonary disease.

The identified patients will be provided with educational material from their community pharmacist and advised to seek a review of their asthma management from their GP. They will be given a letter to be taken to their GP which outlines how many reliever and preventer medications they have had dispensed in the preceding 12 months, along with other medications that have been used in this time period. GPs will be asked to complete an anonymous postal survey to gauge their opinions on this program.

A pilot study demonstrated that the intervention resulted in a three-fold improvement in the preventer-to-reliever ratio of dispensed asthma medications. This project will assess the intervention on a wider scale. Approximately 10 pharmacies in Tasmania will be involved in this program, and it is expected that each pharmacy will provide information to around 20 patients. For further information regarding this project you can contact:-

Dr Shane Jackson (Chief Investigator) on 0408 485 430
shane.jackson@utas.edu.au
or
Bonnie Bereznicki (PhD Candidate) on 6226 2191
bonnie.bereznick@utas.edu.au

3.2.6 Random allocation of intervention type

Each participating pharmacy was randomly assigned to deliver only one type of intervention; mailed or face-to-face. In each state, a complete list of participating pharmacies was created, and pharmacies were sorted according to their distance from

the state's capital city. The first pharmacy on each list was randomly allocated to perform mailed or face-to-face interventions, with subsequent pharmacies being alternately assigned to perform face-to-face or mailed interventions. This type of randomisation process ensured an even geographical spread of pharmacists performing each type of intervention. Furthermore, allocating pharmacies to perform one type of intervention ensured that the pharmacists' preference for one intervention type over another did not influence the uptake.

Pharmacists randomised to perform mailed interventions were to use the MedeMine-for-Asthma program to print personalised letters and coded surveys for eligible intervention patients and their GPs, and mail the intervention packs to patients. Pharmacists randomised to perform face-to-face interventions were to use the MedeMine-for-Asthma program to print personalised letters and coded surveys for eligible intervention patients and their GPs, and hand the intervention packs to patients, with counselling, as they presented to the pharmacy during the intervention period.

3.2.7 The intervention

3.2.7.1 Installation and running the MedeMine-for-Asthma program

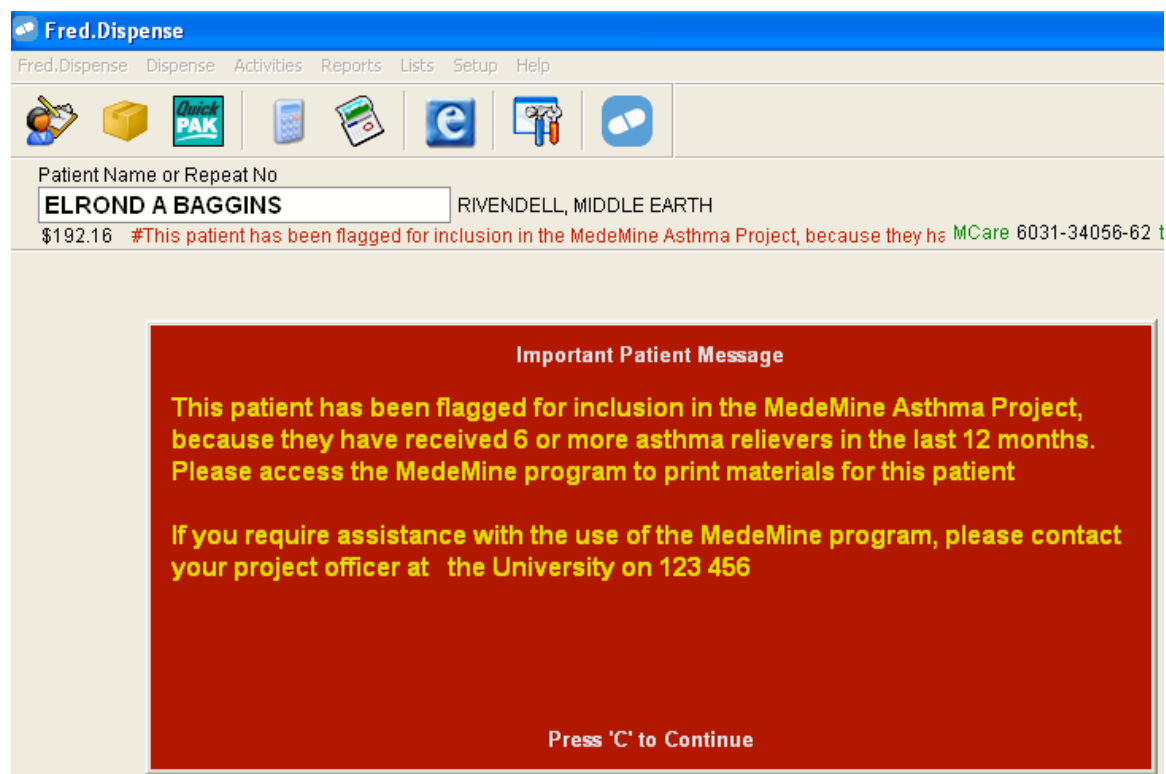
Researchers in Victoria and South Australia were provided with instructions for installing the MedeMine-for-Asthma program on the main dispensing computer in each pharmacy (Appendix 14). Once the software had been installed, pharmacists were advised of the type of intervention they had been allocated to perform, and given instructions on how to use the MedeMine-for-Asthma program to perform the intervention (Appendices 15 and 16).

Upon the installation of the program in each pharmacy, the researcher was required to enter a password depending on the type of intervention the pharmacy had been randomised to perform. The MedeMine-for-Asthma program was engineered to perform specific applications for each type of intervention. For example, the program would allow all patient letters and surveys to be printed at once for the mailed intervention, and then calculate the number printed to determine the amount of money that the pharmacist could claim for postage costs at the end of the intervention period. Patient letters and surveys could only be printed individually for the face-to-face intervention, and postage costs were not added onto the amount of money that the pharmacist could claim

at the end of the intervention period. Having to print letters and surveys individually discouraged pharmacists from printing them all at once and handing them out as the patients presented to the pharmacy. The reasoning for this was that once the letters and surveys had been printed for each patient, the program registered the patient as having received the intervention. Pharmacists were therefore encouraged to print each set of letters and surveys immediately prior to handing to each patient.

As a reminder for pharmacists performing the face-to-face intervention to print and hand out intervention packs to patients as they presented to the pharmacy, the MedeMine-for-Asthma program placed an alert flag in the intervention patients' dispensing information that would appear on the screen when the pharmacist dispensed any medication for that patient (Figure 21). This alert flag would only appear if the password entered after the program was installed indicated that the pharmacy would be performing the face-to-face intervention. Furthermore, the flag was automatically removed from a patient's dispensing information if the pharmacist excluded a patient, or if the letters and surveys for a patient had already been printed.

Figure 21. Example alert flag in Fred Dispense



Before mailing or handing out any intervention packs, the pharmacists were encouraged to examine the dispensing information for the intervention patients and use their

professional judgement, based on their knowledge of each patient, to decide whether the patient was eligible to receive an intervention. The pharmacists were encouraged to include all patients unless they met the pre-defined exclusion criteria, which were listed in a drop-down menu, as shown in Figure 22. Pharmacists who were excluding patients from receiving an intervention were to choose a reason from the list above the black line (primary exclusion reasons), and those who were excluding patients from further participation after they had received an intervention were to choose a reason from the list below the black line (secondary exclusion reasons). In addition, if the pharmacist needed to exclude a patient for any other reason, they could select 'other...' and type the reason.

Figure 22. MedeMine-for-Asthma screenshot showing exclusion criteria

The screenshot shows a window titled "Viewing Asthma trial for Elrond BAGGINS". It features a "Reason for Exclusion" dropdown menu. Below the menu, there are two lists of exclusion reasons separated by a horizontal line. The top list (primary exclusion reasons) includes: "Too confused", "Deceased", "Patient has COPD", "Nursing Home Resident", "May cause undue distress", "Under 18 years old", and "Other ...". The bottom list (secondary exclusion reasons) includes: "Letter returned to sender", "Declines to participate", "Prefers no further contact", "Privacy concerns", and "Other ...". Below these lists, there is a checkbox labeled "You described the project to the patient" and a section titled "Overall, the patient's view of the study is :" with four radio buttons: "Positive", "Negative", "Indifferent", and "Clear". At the bottom, there is a text area labeled "Patient's description of Outcomes of talking with GP about asthma" and two buttons: "Close" and "Reprint Letters".

Pharmacists were blinded to the control patients' identities until the end of the 12-month post-intervention period. In this way, it was intended that control patients would receive no active intervention other than the pharmacist's usual care.

3.2.7.2 The intervention period

The intervention period began in June 2008 and ran for six weeks. Pharmacists performing the mailed intervention were encouraged to mail out all the intervention

packs, and pharmacists performing the face-to-face intervention were encouraged to hand out as many intervention packs as possible, during this time.

The MedeMine-for-Asthma program generated a personalised letter to send to each intervention patient. The contents of the letter indicated that, based on the record of medication that had been dispensed recently, the pharmacist was concerned that the patient's asthma may not be ideally controlled and that it would be advisable for the patient to visit his or her GP for an asthma management review.

Intervention patients were sent an asthma intervention pack containing the following information:

- A MedeMine-for-Asthma-generated personalised letter (Appendix 17);
- Supporting educational material provided by the Asthma Foundations Australia ('Asthma: the basic facts');³¹³
- MedeMine-for-Asthma-generated and uniquely coded asthma control (Appendix 18), quality of life (Appendix 19), and adherence behaviour (Appendix 20) questionnaires, to be self-completed;
- A standard (non-personalised) letter about the surveys (Appendix 21);
- A MedeMine-for-Asthma-generated letter (and medication history) to give to their GP (Appendix 22);
- A standard (non-personalised) letter about the study to give to their GP (Appendix 13); and
- A MedeMine-for-Asthma-generated a uniquely coded satisfaction/perception questionnaire to give to their GP (Appendix 23).

Pharmacists were encouraged to document any feedback received from patients or GPs, or relevant details of the face-to-face intervention in the 'extra information' tab, as displayed in Figure 23. Each time the MedeMine-for-Asthma program was accessed, the de-identified and encrypted dispensing information, as well as additional information entered into the program, was automatically sent via the Internet to a secure server at the University of Tasmania.

Figure 23. MedeMine-for-Asthma screenshot of ‘extra information’ tab

Viewing Asthma trial for Elrond BAGGINS

Elrond BAGGINS
Rivendell
Middle Earth 0

Reason for Exclusion

Initial Letter Printed on: 5/06/2008 3:19:32 PM

Second Letter Printed on: / / : : AM

Seen by GP ☐

Asthma-related Dispensings Collated History All Dispensing History **Extra Information**

Patient's feedback about project

☐ You counselled the patient on their inhaler technique ☐ You recommended the patient ask their GP for an asthma plan

☐ You referred the patient to their GP ☐ You recommended the patient ask their GP for a HMR referral

☐ You described the project to the patient

Overall, the patient's view of the study is :

☐ Positive ☐ Negative ☐ Indifferent ☐ Clear

Patient's description of Outcomes of talking with GP about asthma

Close Reprint Letters

3.2.7.3 Support for pharmacists

Pharmacists were encouraged to contact their local researcher if they had any queries or concerns relating to the study. In addition, a researcher telephoned all pharmacists every two weeks throughout the intervention period, to ask how the study was progressing and offer advice and support if needed.

3.2.8 Questionnaire instruments

3.2.8.1 Asthma Control Test

The Asthma Control Test (ACT)⁶⁰ is a validated 5-item test designed to measure the patient's level of asthma control during the preceding four weeks (only two weeks was used in this study, in an attempt to be consistent with the Mini Asthma Quality of Life Questionnaire). Items relate to use of reliever medication, shortness of breath, night-time symptoms, activity limitation and self-assessed asthma control. Each item contains a 5-point scale where 5 = completely controlled and 1 = not at all controlled, and the overall score out of 25 is given by the addition of the response to each item. Patients were also asked to indicate their gender, age group (< 18, 18-29, 30-39, 40-49, 50-59 or ≥ 60 years) and whether or not they possessed a written AAP. These parameters were

added on to the end of the shortest questionnaire (the Asthma Control Test) for convenience.

3.2.8.2 Mini Asthma Quality of Life Questionnaire

The Mini Asthma Quality of Life Questionnaire (MiniAQLQ) is a validated 15-item questionnaire designed to measure the patient's perspective of the impact of asthma on their QOL during the preceding two weeks.³⁴⁷ The MiniAQLQ contains items relating to symptom severity (shortness of breath, difficulty in sleeping and chest tightness, coughing and wheezing), the effect on emotional function (frustration, concern and fear), the effect of environmental stimuli (dust and cigarette smoke) and limitation of activities (strenuous, moderate, social and work-related activities). Each item contains a 7-point-scale where 7 = no impairment and 1 = maximum impairment, and the overall score was given by the average value for the response to the items. Each domain of the questionnaire allows for calculation of separate scores for symptoms, emotions, environment and activities, as well as the overall QOL score.

3.2.8.3 Tool for Adherence Screening Behaviour

The Tool for Adherence Behaviour Screening (TABS) is a validated scale that screens both intentional and unintentional non-adherence to pharmacological and non-pharmacological disease management.³⁴⁸ The TABS measures adherent and non-adherent behaviour on five-point Likert-type scales, with higher scores indicating higher degrees of adherent and non-adherent behaviour. Adherence items relate to having a strict routine for using medications, keeping medications close to where they are needed, having enough medication so that they don't run out and pushing oneself to following the doctor's instructions. Non-adherence items relate to getting confused about one's medications, making changes to the recommended management to suit one's lifestyle, varying the recommended management based on how one is feeling and putting up with medical problems before taking any action. The items used in the TABS were developed based on common adherence issues experienced by a sample of chronically ill patients and cover domains, judged by experts, to be important in adherence screening.³⁴⁸

3.2.8.4 GP survey

There were two parts to the GP survey. The first part contained three questions, and was patient-specific, focusing on (i) any modifications made in regards the patient's asthma therapy, (ii) whether the GP felt that the patient was appropriately identified as needing a review of their asthma therapy and (iii) whether the GP agreed that the patient would benefit from the intervention. The second part of the questionnaire assessed the GP's opinions on the usefulness of the project and of projects such as this one. Specifically, it assessed whether the GP agreed that (i) pharmacists are well placed to identify patients who may need review of their asthma therapy, (ii) there is an evident need for improved asthma management in the community and (iii) this type of program delivered by community pharmacists would be likely to improve asthma care in the community if implemented on a larger scale.

3.2.8.5 Pharmacist satisfaction survey

Pharmacists were asked to complete a satisfaction survey (Appendix 24) at the end of the six-week intervention period. The survey questions assessed the pharmacists' beliefs about the evident need for, the appropriateness of and the effectiveness of the intervention, as well issues relating to implementation of the intervention in usual practice.

3.2.8.6 Patient satisfaction survey

All included intervention patients were sent a satisfaction survey (Appendix 25) at the end of the post-intervention period. The questions assessed the perceived usefulness and appropriateness of the intervention, as well as the satisfaction with the level of asthma care usually received by doctors and community pharmacists.

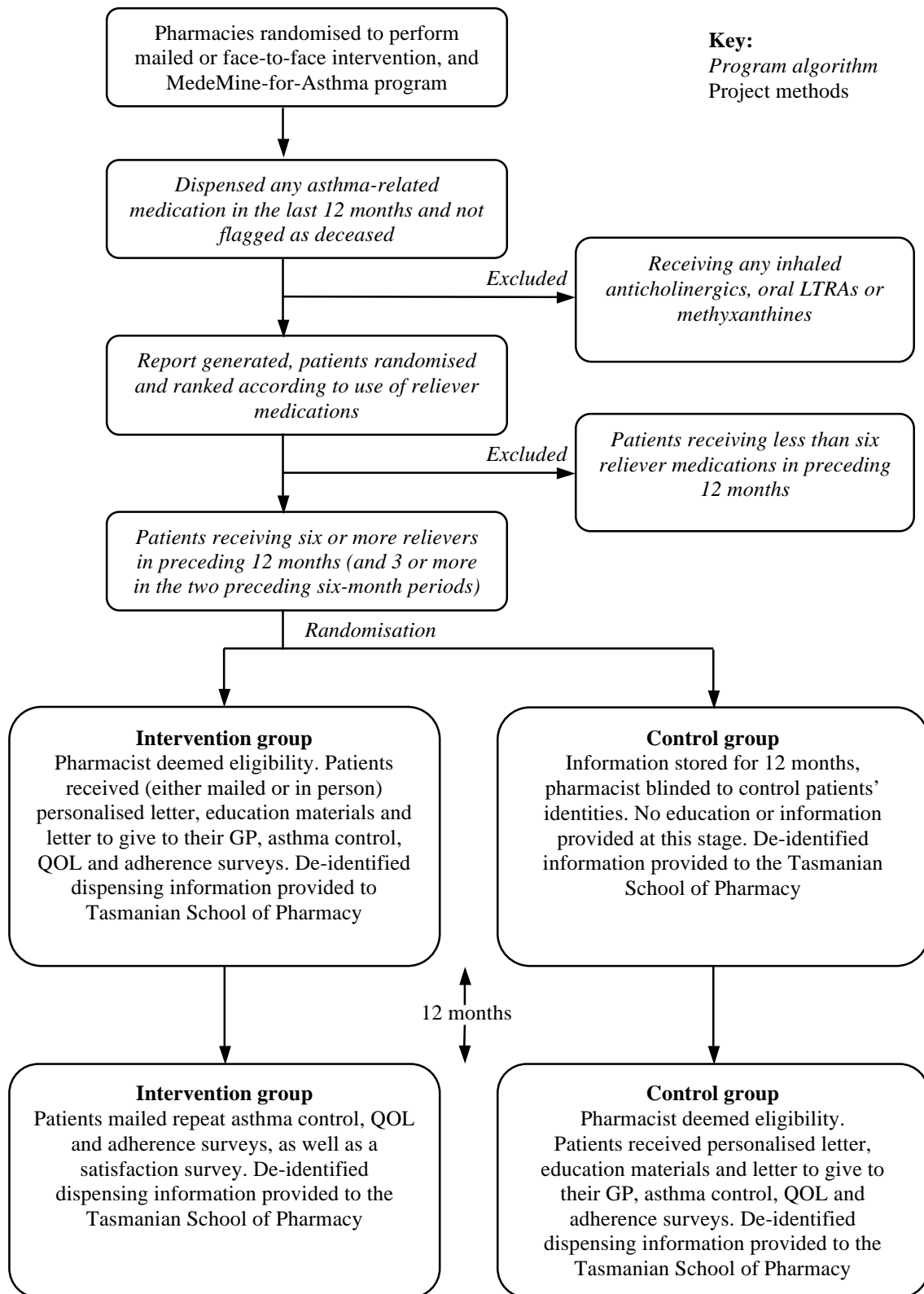
3.2.9 Post-intervention follow-up

Twelve months after the intervention, the researchers in Victoria and South Australia were provided with instructions for the post-intervention site visits (Appendix 26). The control patients' identities were revealed, and pharmacists examined their dispensing information to determine whether they were eligible to be included in the study (that is, they did not meet any of the exclusion criteria). For ethical reasons, all included control patients who had received six or more relievers in the post-intervention period were sent an intervention pack, the same as that sent to intervention patients 12 months earlier.

Control patients who received less than six relievers in the post-intervention period were not sent an intervention pack, but their dispensing data were still included in the analyses, because they were otherwise eligible to remain in the study.

Intervention patients received a follow-up letter (Appendix 27), and were again provided with the three questionnaires on asthma control, asthma-related QOL and medication adherence behaviour knowledge, as well as a satisfaction questionnaire. Figure 24 displays a summary of the project's methodology.

Figure 24. Summary of the project's methodology



3.2.10 Handling of data and statistical analysis

All surveys and dispensing data were de-identified. Patient and GP surveys were coded with unique identification numbers that could be linked to patients' dispensing data, but could not be re-identified by the researchers.

The asthma medications included in the analyses were inhaled SABAs (relievers) and ICS (preventers). Prior to performing statistical analyses, the dispensed quantities of asthma medications were converted to a standard equivalent dose:

- Salbutamol equivalence: salbutamol 100 µg = terbutaline 250 µg;³¹⁵ and
- Beclomethasone-HFA equivalence: beclomethasone-HFA 100 µg = fluticasone 100 µg = budesonide 200 µg = ciclesonide 80 µg.¹³⁴⁻¹³⁶

Because eformoterol can now be prescribed as a reliever, as part of the Symbicort[®] Maintenance And Reliever Therapy regimen, it was counted as a reliever (with 3 µg of eformoterol equivalent to 100 µg of salbutamol)³⁴⁹ if the dispensing instructions indicated it was being used in this manner.

The preventer-to-reliever (P : R) ratio was calculated for each patient as the average beclomethasone-equivalent usage per day divided by the average salbutamol-equivalent usage per day. The primary outcome measure was the P : R ratio of dispensed asthma medication, and secondary outcome measures were other patterns in dispensed asthma medication, asthma questionnaire scores and participant satisfaction.

All variables were collated and entered into a statistical software package, Statview 5.01 (Abacus Concepts Inc, Berkeley, California, USA). Parametric data are presented as means \pm standard deviations, and nonparametric data are presented as medians (interquartile ranges). Within-group comparisons of dispensing data were conducted using the Wilcoxon signed-rank test, and between-group comparisons were conducted using the Kruskal-Wallis test. Post hoc testing was performed using the Mann Whitney test with Bonferroni correction. The Bonferroni adjusted critical value controlled for multiple comparison testing, and was obtained by dividing the original threshold *P* value (0.05) by the total number of comparisons made (three).^{322,323}

The dispensing data was analysed using the treatment-received method, whereby only patients who received the intervention were compared to controls. To account for

uptake of the intervention by pharmacists, the dispensing data was also analysed using the intention-to-treat method, whereby all eligible patients were analysed for changes in dispensing data.

Within group comparisons of asthma questionnaire scores were conducted using the paired Student's *t*-test, and each intervention group was compared to the control group using the unpaired Student's *t*-test. Proportional data were analysed using the χ^2 test. A significance level of $P < 0.05$ was used for all statistical procedures, with the exception of the post hoc Mann Whitney test, in which a Bonferroni adjusted significance level of $P < 0.0167$ was used.^{322,323}

3.2.11 Ethical approval and trial registration

This project received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee (ethics reference number H9823), Monash University's Human Research Ethics Committee (ethics reference number 2008000274) and the University of South Australia's Human Research Ethics Committee (ethics reference number P056/08). The study was registered with the Australian New Zealand Clinical Trial Registry (registration number ACTRN12608000119392).

3.3 Results

3.3.1 Participants

3.3.1.1 Recruitment of pharmacies

A total of 459 pharmacies were invited to participate in the study by telephone and mail. Table 24 displays the responses of pharmacists to the expression of interest form and follow-up telephone calls.

Table 24. Pharmacists' willingness to participate

Response	Pharmacies contacted			
	All states (n = 459)	Tasmania (n = 69)	Victoria (n = 163)	South Australia (n = 227)
Use the Fred dispensing system and willing to participate	71 (15.5%)	9 (13.0%)	37 (22.7%)	25 (11.0%)
Do not use the Fred dispensing system	231 (50.3%)	53 (76.8%)	35 (21.5%)	143 (63.0%)
Use the Fred dispensing system, but do not feel able to participate	157 (34.2%)	7 (10.1%)	91 (55.8%)	59 (26.0%)

Of the 71 pharmacies that agreed to participate, 36 (50.7%) were randomised to perform the mailed intervention, and 35 (49.3%) were randomised to perform the face-to-face intervention.

3.3.1.2 Identification of patients

The stepwise identification of patients is shown in Table 25. Total patient numbers were available for 62 (87.3%) of the 71 pharmacies. Each pharmacy database contained an average of 6,461 patients. Of these patients, an average of 548 (8.5%) were identified as having received one or more reliever canister in the past 12 months, excluding those who had received methylxanthines, inhaled anticholinergics or leukotriene receptor antagonists). Of these patients, an average of 23 (4.2%) were identified as having received six or more reliever canisters in the past 12 months, with three or more in both of the two previous six-month periods.

Table 25. Stepwise identification of patients

Pharmacy ID	State	Total patients in pharmacy database	Patients dispensed ≥ 1 reliever in past 12 months ^{*†}	Patients dispensed ≥ 6 relievers in past 12 months [†]
1	Tas	16,717	1,527 (9.1%)	47 (3.1%)
2	Tas	1,225	134 (10.9%)	12 (9.0%)
3	Tas	3,482	359 (10.3%)	21 (5.8%)
4	Tas	12,723	895 (7.0%)	25 (2.8%)
5	Tas	5,278	323 (6.1%)	9 (2.8%)
6	Tas	4,163	339 (8.1%)	20 (5.9%)
7	Tas	4,913	588 (12.0%)	37 (6.3%)
8	Tas	14,126	1,346 (9.5%)	21 (1.6%)
9	Tas	13,534	1,332 (9.8%)	59 (4.4%)
10	Vic	2,608	198 (7.6%)	9 (4.5%)
11	Vic	N/A	N/A	10
12	Vic	7,977	558 (7.0%)	47 (8.4%)
13	Vic	7,144	872 (12.2%)	64 (7.3%)
14	Vic	1,574	202 (12.8%)	13 (6.4%)
15	Vic	3,271	227 (6.9%)	26 (11.5%)
16	Vic	2,579	205 (7.9%)	7 (3.4%)
17	Vic	4,445	404 (9.1%)	14 (3.5%)
18	Vic	6,689	757 (11.3%)	37 (4.9%)
19	Vic	3,822	233 (6.1%)	6 (2.6%)
20	Vic	16,391	1,741 (10.6%)	45 (2.6%)
21	Vic	8,662	750 (8.7%)	18 (2.4%)
22	Vic	2,516	190 (7.6%)	4 (2.1%)
23	Vic	2,781	206 (7.4%)	15 (7.3%)
24	Vic	5,463	357 (6.5%)	8 (2.2%)
25	Vic	14,453	959 (6.6%)	8 (0.8%)
26	Vic	3,305	198 (6.0%)	4 (2.0%)
27	Vic	1,402	108 (7.7%)	9 (8.3%)
28	Vic	4,680	257 (5.5%)	9 (3.5%)
29	Vic	3,299	378 (11.5%)	16 (4.2%)
30	Vic	3,094	255 (8.2%)	10 (3.9%)
31	Vic	13,682	1,034 (7.6%)	27 (2.6%)
32	Vic	16,200	1,076 (6.6%)	42 (3.9%)
33	Vic	N/A	N/A	26
34	Vic	N/A	N/A	17
35	Vic	3,765	274 (7.3%)	11 (4.0%)
36	Vic	4,533	383 (8.4%)	17 (4.4%)

37	Vic	9,285	571 (6.1%)	9 (1.6%)
38	Vic	4,583	511 (11.1%)	36 (7.0%)
39	Vic	4,204	338 (8.0%)	13 (3.8%)
40	Vic	17,130	1228 (7.2%)	39 (3.2%)
41	Vic	N/A	N/A	12
42	Vic	N/A	N/A	22
43	Vic	5,961	482 (8.1%)	36 (7.5%)
44	Vic	3,777	203 (5.4%)	5 (2.5%)
45	Vic	3,379	294 (8.7%)	10 (3.4%)
46	Vic	8,815	472 (5.4%)	16 (3.4%)
47	SA	2,564	245 (9.6%)	16 (6.5%)
48	SA	N/A	N/A	5
49	SA	1,385	186 (13.4%)	18 (9.7%)
50	SA	N/A	N/A	45
51	SA	1,259	119 (9.5%)	3 (2.5%)
52	SA	4,157	365 (8.8%)	26 (7.1%)
53	SA	11,353	1111 (9.8%)	59 (5.3%)
54	SA	6,443	663 (10.3%)	36 (5.4%)
55	SA	8,886	844 (9.5%)	32 (3.8%)
56	SA	4,207	339 (8.1%)	13 (3.8%)
57	SA	16,216	1,548 (9.5%)	55 (3.6%)
58	SA	5,958	692 (11.6%)	45 (6.5%)
59	SA	6,541	485 (7.4%)	17 (3.5%)
60	SA	5,481	466 (8.5%)	12 (2.6%)
61	SA	2,922	308 (10.5%)	21 (6.8%)
62	SA	3,112	271 (8.7%)	9 (3.3%)
63	SA	10,261	988 (9.6%)	28 (2.8%)
64	SA	N/A	N/A	12
65	SA	13,080	995 (7.6%)	17 (1.7%)
66	SA	5,905	534 (9.0%)	14 (2.6%)
67	SA	1,948	207 (10.6%)	8 (3.9%)
68	SA	N/A	N/A	5
69	SA	2,788	201 (7.2%)	3 (1.5%)
70	SA	1,951	159 (8.1%)	4 (2.5%)
71	SA	6,553	481 (7.3%)	12 (2.5%)

*Excluding patients who had received any methylxanthines, inhaled anticholinergics or leukotriene receptor antagonists. †Figures represent number of patients (percent of number in column to the left).

The MedeMine-for-Asthma program identified a total of 1,483 patients (510 [34.4%] mailed intervention patients, 480 [32.4%] face-to-face intervention patients and 493 [33.2%] control patients) from 71 pharmacies. Table 26 displays the number of patients identified in each pharmacy.

Table 26. Patients identified in each pharmacy

Pharmacy ID	State	Intervention type	Patients identified* (n = 1483)	Intervention [†] (n = 990)	Control [†] (n = 493)
1	Tas	Face-to-face	47 (3.2%)	31 (66.0%)	16 (34.0%)
2	Tas	Mailed	12 (0.8%)	8 (66.7%)	4 (33.3%)
3	Tas	Face-to-face	21 (1.4%)	14 (66.7%)	7 (33.3%)
4	Tas	Face-to-face	25 (1.7%)	17 (68.0%)	8 (32.0%)
5	Tas	Mailed	9 (0.6%)	6 (66.7%)	3 (33.3%)
6	Tas	Mailed	20 (1.3%)	14 (70.0%)	6 (30.0%)
7	Tas	Mailed	37 (2.5%)	25 (67.6%)	12 (32.4%)
8	Tas	Face-to-face	21 (1.4%)	14 (66.7%)	7 (33.3%)
9	Tas	Mailed	59 (4.0%)	40 (67.8%)	19 (32.2%)
10	Vic	Face-to-face	9 (0.6%)	6 (66.7%)	3 (33.3%)
11	Vic	Mailed	10 (0.7%)	7 (70.0%)	3 (30.0%)
12	Vic	Mailed	47 (3.2%)	31 (66.0%)	16 (34.0%)
13	Vic	Face-to-face	64 (4.3%)	42 (65.6%)	22 (34.4%)
14	Vic	Face-to-face	13 (0.9%)	9 (69.2%)	4 (30.8%)
15	Vic	Mailed	26 (1.8%)	17 (65.4%)	9 (34.6%)
16	Vic	Face-to-face	7 (0.5%)	5 (71.4%)	2 (28.6%)
17	Vic	Face-to-face	14 (0.9%)	9 (64.3%)	5 (35.7%)
18	Vic	Mailed	37 (2.5%)	25 (67.6%)	12 (32.4%)
19	Vic	Face-to-face	6 (0.4%)	4 (66.7%)	2 (33.3%)
20	Vic	Mailed	45 (3.0%)	30 (66.7%)	15 (33.3%)
21	Vic	Face-to-face	18 (1.2%)	12 (67.7%)	6 (33.3%)
22	Vic	Mailed	4 (0.3%)	3 (75.0%)	1 (25.0%)
23	Vic	Mailed	15 (1.0%)	10 (66.7%)	5 (33.3%)
24	Vic	Mailed	8 (0.5%)	5 (62.5%)	3 (37.5%)
25	Vic	Mailed	8 (0.5%)	5 (62.5%)	3 (37.5%)
26	Vic	Face-to-face	4 (0.3%)	3 (75.0%)	1 (25.0%)
27	Vic	Face-to-face	9 (0.6%)	6 (66.7%)	3 (33.3%)
28	Vic	Face-to-face	9 (0.6%)	6 (66.7%)	3 (33.3%)
29	Vic	Face-to-face	16 (1.1%)	10 (62.5%)	6 (37.5%)
30	Vic	Mailed	10 (0.7%)	7 (70.0%)	3 (30.0%)
31	Vic	Mailed	27 (1.8%)	18 (66.7%)	9 (33.3%)
32	Vic	Face-to-face	42 (2.8%)	28 (66.7%)	14 (33.3%)
33	Vic	Face-to-face	26 (1.8%)	17 (65.4%)	9 (34.6%)
34	Vic	Mailed	17 (1.1%)	11 (64.7%)	6 (35.3%)
35	Vic	Face-to-face	11 (0.7%)	7 (63.6%)	4 (36.4%)
36	Vic	Mailed	17 (1.1%)	12 (70.6%)	5 (29.4%)

37	Vic	Mailed	9 (0.6%)	6 (66.7%)	3 (33.3%)
38	Vic	Face-to-face	36 (2.4%)	24 (66.7%)	12 (33.3%)
39	Vic	Face-to-face	13 (0.9%)	9 (69.2%)	4 (30.8%)
40	Vic	Mailed	39 (2.6%)	26 (66.7%)	13 (33.3%)
41	Vic	Mailed	12 (0.8%)	8 (66.7%)	4 (33.3%)
42	Vic	Mailed	22 (1.5%)	15 (68.2%)	7 (31.8%)
43	Vic	Mailed	36 (2.4%)	24 (66.7%)	12 (33.3%)
44	Vic	Mailed	5 (0.3%)	4 (80.0%)	1 (20.0%)
45	Vic	Face-to-face	10 (0.7%)	7 (70.0%)	3 (30.0%)
46	Vic	Face-to-face	16 (1.1%)	10 (62.5%)	6 (37.5%)
47	SA	Face-to-face	16 (1.1%)	11 (68.8%)	5 (31.3%)
48	SA	Mailed	5 (0.3%)	4 (80.0%)	1 (20.0%)
49	SA	Mailed	18 (1.2%)	12 (67.7%)	6 (33.3%)
50	SA	Face-to-face	45 (3.0%)	30 (66.7%)	15 (33.3%)
51	SA	Mailed	3 (0.2%)	2 (66.7%)	1 (33.3%)
52	SA	Mailed	26 (1.8%)	17 (65.4%)	9 (34.6%)
53	SA	Mailed	59 (4.0%)	39 (66.1%)	20 (33.9%)
54	SA	Face-to-face	36 (2.4%)	24 (66.7%)	12 (33.3%)
55	SA	Mailed	32 (2.2%)	21 (65.6%)	11 (34.4%)
56	SA	Face-to-face	13 (0.9%)	8 (61.5%)	5 (38.5%)
57	SA	Face-to-face	55 (3.7%)	37 (67.3%)	18 (32.7%)
58	SA	Mailed	45 (3.0%)	30 (66.7%)	15 (33.3%)
59	SA	Face-to-face	17 (1.1%)	11 (64.7%)	6 (35.3%)
60	SA	Face-to-face	12 (0.8%)	8 (66.7%)	4 (33.3%)
61	SA	Face-to-face	21 (1.4%)	14 (66.7%)	7 (33.3%)
62	SA	Mailed	9 (0.6%)	6 (66.7%)	3 (33.3%)
63	SA	Face-to-face	28 (1.9%)	18 (64.3%)	10 (35.7%)
64	SA	Mailed	12 (0.8%)	8 (66.7%)	4 (33.3%)
65	SA	Face-to-face	17 (1.1%)	11 (64.7%)	6 (35.3%)
66	SA	Face-to-face	14 (0.9%)	10 (71.4%)	4 (28.6%)
67	SA	Face-to-face	8 (0.5%)	5 (62.5%)	3 (37.5%)
68	SA	Mailed	5 (0.3%)	4 (80.0%)	1 (20.0%)
69	SA	Mailed	3 (0.2%)	2 (66.7%)	1 (33.3%)
70	SA	Face-to-face	4 (0.3%)	3 (75.0%)	1 (25.0%)
71	SA	Mailed	12 (0.8%)	8 (66.7%)	4 (33.3%)

*Figures represent number (%) of total patients identified. †Figures represent number (%) of total patients identified in each pharmacy.

3.3.1.3 Patient exclusions

Of the 510 mailed intervention patients identified, 47 (9.2%) were excluded from the study, leaving 463 (90.8%) patients eligible to receive an intervention. Of the 480 face-to-face intervention patients identified, 38 (7.9%) were excluded from the study, leaving 442 (92.1%) patients eligible to receive an intervention. Of the 493 control patients identified, 59 (12.0%) were excluded from the study, leaving 434 (88.0%) control patients. Table 27 displays the reasons for patient exclusion by pharmacists.

Table 27. Reasons for patient exclusion

Reason for exclusion	All patients (n = 144)	Mailed intervention (n = 47)	Face-to-face intervention (n = 38)	Control (n = 59)
Under 18 years old*	30 (20.8%)	16 (34.0%)	7 (18.4%)	7 (11.9%)
Patient has COPD*	27 (18.8%)	2 (4.3%)	2 (5.3%)	23 (39.0%)
Too confused*	26 (18.1%)	6 (12.8%)	6 (15.8%)	14 (23.7%)
Nursing home resident*	17 (11.8%)	5 (10.6%)	8 (21.1%)	4 (6.8%)
May cause undue distress*	14 (9.7%)	6 (12.8%)	3 (7.9%)	5 (8.5%)
No longer a regular patient	12 (8.3%)	9 (19.1%)	1 (2.6%)	2 (3.4%)
Doctor's bag / first aid kit	9 (6.3%)	1 (2.1%)	6 (15.8%)	2 (3.4%)
Other medical condition	5 (3.5%)	1 (2.1%)	3 (7.9%)	1 (1.7%)
Deceased*	3 (2.1%)	1 (2.1%)	1 (2.6%)	1 (1.7%)
Under specialist care	1 (0.7%)	0 (0.0%)	1 (2.6%)	0 (0.0%)

*Pre-defined exclusion criteria.

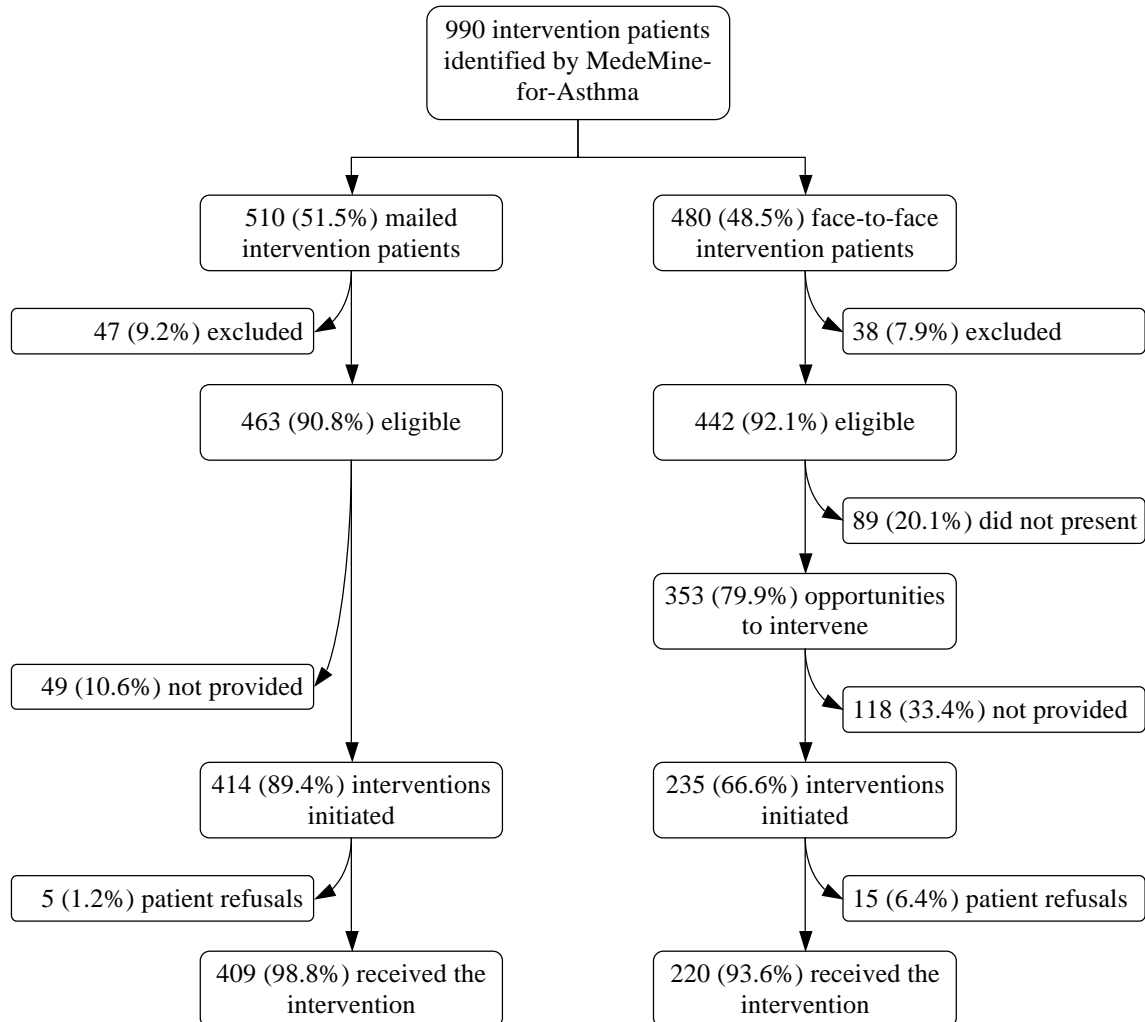
3.3.2 Uptake of the intervention

Of the 463 patients who were eligible for a mailed intervention, 414 (89.4%) were sent an intervention pack by their pharmacist. Of the 442 patients who were eligible for a face-to-face intervention, 235 (53.2%) were offered an intervention pack by their pharmacist. Of the 207 patients who were not offered a face-to-face intervention, 118 (57.0%) patients had at least one prescription dispensed during the intervention period, whereas 89 (43.0%) did not present to the pharmacy during the intervention period. Therefore, a total of 353 face-to-face intervention patients presented to the pharmacy during the intervention period, of which 235 (66.6%) were offered an intervention, and 118 (33.4%) were not.

Taking opportunity to intervene into account, significantly fewer face-to-face intervention patients were offered an intervention, compared with mailed intervention

patients (66.6% versus 89.4%, respectively; $\chi^2 = 64.2$, $P < 0.0001$). Figure 25 displays the uptake of the mailed and face-to-face interventions by pharmacists.

Figure 25. Uptake of the intervention by pharmacists



3.3.3 Patient and GP survey response rates

Of the 409 patients who received a mailed intervention, 34 (8.3%) returned the baseline surveys and 60 (14.7%) returned the post-intervention surveys. Of the 34 patients who responded to the baseline surveys, 11 (32.4%) responded again to the post-intervention surveys. Of the 409 patients who received a mailed intervention (which included a survey to hand to their GP), a total of 14 (3.4%) GPs completed and returned a GP evaluation survey. Out of 34 completed baseline patient surveys, 11 (32.4%) could be linked to their corresponding GP surveys. There were three GP surveys returned which did not have a corresponding patient survey.

Of the 230 patients who received a face-to-face intervention, 40 (17.4%) returned the baseline surveys and 48 (20.9%) returned the post-intervention surveys. Of the 40 patients who responded to the baseline surveys, 18 (45.0%) responded again to the post-intervention surveys. Of the 230 patients who received a face-to-face intervention, a total of 20 (8.7%) GPs completed and returned a GP evaluation survey. Out of 40 completed baseline patient surveys, 19 (47.5%) could be linked to their corresponding GP surveys. There was one GP survey returned which did not have a corresponding patient survey.

Of the 434 control patients, 334 (77.0%) had received six or more relievers in the post-intervention period, and were sent a mailed intervention at the end of the study period. Of the 334 control patients who received an intervention, 18 (5.4%) returned the questionnaires. Of the 334 control patients who received an intervention, a total of 14 (4.2%) GPs completed and returned a GP evaluation questionnaire. Out of 18 completed patient questionnaires, 10 (55.6%) could be linked to their corresponding GP questionnaires. There were four GP questionnaires returned which did not have a corresponding patient questionnaire.

Overall, the average patient questionnaire return rate was 13.3%, and the average GP questionnaire return rate was 5.4%.

3.3.4 Patient demographics

The mailed intervention, face-to-face intervention and control patients were well matched with respect to demographic measures. No significant differences were observed between the three groups in terms of age or gender, as displayed in Table 28.

Table 28. Patient demographic variables

Parameter	All patients (n = 171)	Mailed intervention (n = 83)	Face-to-face intervention (n = 70)	Control (n = 18)	P
<i>Age (years)</i>					0.79
<18	3 (1.8%)	1 (1.2%)	2 (2.9%)	0 (0.0%)	
18-29	8 (4.7%)	5 (6.0%)	2 (2.9%)	1 (5.6%)	
30-39	5 (2.9%)	3 (3.6%)	2 (2.9%)	0 (0.0%)	
40-49	21 (7.0%)	10 (12.0%)	10 (14.3%)	1 (5.6%)	
50-59	27 (12.3%)	13 (15.7%)	13 (18.6%)	1 (5.6%)	
≥60	107 (62.6%)	51 (61.4%)	41 (58.6%)	15 (83.3%)	
<i>Gender</i>					0.43
Male	80 (46.8%)	37 (44.6%)	32 (45.7%)	11 (61.1%)	
Female	91 (53.2%)	46 (55.4%)	38 (54.3%)	7 (38.9%)	

3.3.5 Outcome measures

3.3.5.1 Dispensing data

Using the treatment-received method of analysis, there were significant improvements in the P : R ratio in both intervention groups and the control group, after the intervention (Table 29). The magnitude of improvement in the face-to-face intervention group was greater than that in the mailed intervention group, which was greater than that in the control group ($Z = -5.38, -5.16$ and -4.56 respectively). The improvement in the P : R ratios were mainly due to significant decreases in the daily SABA usage within each group. There were no significant changes in the daily ICS usage in the mailed or face-to-face intervention group. However, there were significant increases in the daily ICS usage in the control group.

Table 29. Pre- and post-intervention dispensing data (treatment-received analysis)

Asthma medication	Pre-intervention	Post intervention	<i>P</i>	<i>Z</i>
<i>P : R ratio</i>				
Mailed intervention	0.15 (0.00 - 0.42)	0.19 (0.00 - 0.55)	< 0.0001	-5.16
Face-to-face intervention	0.15 (0.00 - 0.46)	0.21 (0.00 - 0.75)	< 0.0001	-5.38
Control	0.14 (0.00 - 0.42)	0.16 (0.00 - 0.50)	< 0.0001	-4.56
Kruskal-Wallis <i>P</i>	0.68	0.46		
<i>Daily SABA usage (µg)</i>				
Mailed intervention	655.7 (546.5 - 983.6)	563.4 (328.8 - 966.8)	< 0.0001	-6.92
Face-to-face intervention	765.0 (546.5 - 1092.9)	657.5 (329.9 - 1043.0)	< 0.0001	-6.26
Control	655.7 (546.5 - 983.6)	634.9 (339.0 - 987.3)	< 0.0001	-5.74
Kruskal-Wallis <i>P</i>	0.03	0.07		
<i>Daily ICS usage (µg)</i>				
Mailed intervention	123.0 (0.0 - 327.9)	103.0 (0.0 - 354.0)	0.48	-0.70
Face-to-face intervention	118.5 (0.0 - 375.7)	164.4 (0.0 - 422.0)	0.14	-1.48
Control	95.9 (0.0 - 327.9)	102.3 (0.0 - 359.6)	0.03	-2.17
Kruskal-Wallis <i>P</i>	0.44	0.62		

The absolute changes in daily SABA and ICS usage after the intervention (using the treatment-received method of analysis) are displayed in Table 30. There was a difference of borderline significance in the absolute change in SABA usage between the three groups ($df = 2$, $H = 5.29$, $P = 0.07$). Post hoc Mann-Whitney tests showed that there was (i) a non-significant trend (borderline significance) for the change in SABA usage in the mailed intervention patients to be greater than control ($Z = -1.79$, $P = 0.07$), (ii) a non-significant trend for the change in SABA usage in the face-to-face intervention patients to be greater than control ($Z = -2.19$, $P = 0.03$ [Bonferroni adjusted significance level of $P < 0.0167$]), and (iii) no significant difference in the absolute change in SABA usage between the mailed and face-to-face interventions. There was no significant difference in the absolute change in ICS usage between the three groups.

Table 30. Absolute change in daily SABA and ICS usage (treatment-received analysis)

Patient group	Change in daily SABA usage	Change in daily ICS usage
Mailed intervention	-159.5 (-393.0 - 92.0)	0.0 (-64.6 - 69.8)
Face-to-face intervention	-170.0 (-421.00 - 22.8)	0.0 (-53.3 - 84.3)
Control	-99.0 (-3223.5 - 106.0)	0.0 (-49.1 - 83.7)
Kruskal-Wallis <i>P</i>	0.07	0.57

Using the intention-to-treat method of analysis, there were significant improvements in the P : R ratio in both intervention groups and the control group, after the intervention (Table 31). The magnitude of improvement in the mailed intervention group was greater than that in the control group, which was greater than that in the face-to-face intervention group ($Z = -5.41, -4.56$ and -2.77 , respectively). The improvement in the P : R ratios were mainly due to significant decreases in the daily SABA usage within each group. There was no significant change in the daily ICS usage in the mailed intervention group. However, there was a non-significant trend for the daily ICS usage to increase after the face-to-face intervention, and a significant increase in the daily ICS usage in the control group.

Table 31. Pre- and post-intervention dispensing data (intention-to-treat analysis)

Asthma medication	Pre-intervention	Post intervention	<i>P</i>	<i>Z</i>
<i>P : R ratio</i>				
Mailed intervention	0.15 (0.00 - 0.44)	0.20 (0.00 - 0.58)	< 0.0001	-5.41
Face-to-face intervention	0.12 (0.00 - 0.42)	0.16 (0.00 - 0.69)	0.006	-2.77
Control	0.14 (0.00 - 0.42)	0.16 (0.00 - 0.50)	< 0.0001	-4.56
Kruskal-Wallis <i>P</i>	0.54	0.68		
<i>Daily SABA usage (µg)</i>				
Mailed intervention	655.7 (546.5 - 983.6)	549.5 (219.2 - 788.7)	< 0.0001	-7.49
Face-to-face intervention	655.7 (546.5 - 1005.5)	593.8 (328.8 - 967.3)	< 0.0001	-8.04
Control	655.7 (546.5 - 983.6)	634.9 (339.0 - 987.3)	< 0.0001	-5.74
Kruskal-Wallis <i>P</i>	0.62	0.25		
<i>Daily ICS usage (µg)</i>				
Mailed intervention	109.3 (0.0 - 327.9)	102.7 (0.0 - 353.7)	0.47	-0.73
Face-to-face intervention	82.0 (0.0 - 327.9)	110.4 (0.0 - 394.7)	0.08	-1.73
Control	95.9 (0.0 - 327.9)	102.3 (0.0 - 359.6)	0.03	-2.17
Kruskal-Wallis <i>P</i>	0.48	0.95		

The absolute changes in daily SABA and ICS usage after the intervention (using the intention-to-treat method of analysis) are displayed in Table 32. There was a difference of borderline significance in the absolute change in SABA usage between the three groups ($df = 2$, $H = 4.84$, $P = 0.09$). Post hoc Mann-Whitney tests showed that there was (i) a non-significant trend (borderline significance) for the change in SABA usage in the mailed intervention patients to be greater than control ($Z = -1.90$, $P = 0.06$), (ii) a non-significant trend (borderline significance) for the change in SABA usage in the face-to-face intervention patients to be greater than control ($Z = -1.93$, $P = 0.05$), and (iii) no significant difference in the absolute change in SABA usage between the mailed and face-to-face interventions. There was no significant difference in the absolute change in ICS usage between the three groups.

Table 32. Absolute change in daily SABA and ICS usage (intention-to-treat analysis)

Patient group	Change in daily SABA usage	Change in daily ICS usage
Mailed intervention	-162.0 (-387.5 - 91.5)	0.00 (-64.1 - 68.0)
Face-to-face intervention	-145.0 (-421.0 - 46.3)	0.00 (-52.9 - 83.4)
Control	-99.0 (-323.5 - 106.0)	0.00 (-53.9 - 82.2)
Kruskal-Wallis P	0.09	0.66

3.3.5.2 Patient-reported outcomes

There were no significant improvements in patient-reported asthma control, quality of life or medication adherence behaviour after the intervention (Table 33). However, there was a non-significant trend for improved asthma control after the face-to-face intervention ($t = -1.8$, $P = 0.09$). There was also a significant increase in the proportion of patients who possessed written AAPs after the face-to-face intervention ($\chi^2 = 4.0$, $P < 0.05$), but not after the mailed intervention.

Table 33. Pre- and post-intervention asthma survey results

Patient-reported outcome	Pre-intervention	Post intervention	<i>P</i>
<i>Asthma control</i>			
Mailed intervention	18.3 ± 4.3	17.9 ± 4.1	0.20
Face-to-face intervention	16.5 ± 4.8	17.2 ± 4.7	0.09
<i>Quality of life - symptoms</i>			
Mailed intervention	4.9 ± 1.3	4.9 ± 1.1	0.51
Face-to-face intervention	4.6 ± 1.4	4.7 ± 1.4	0.70
<i>Quality of life - emotions</i>			
Mailed intervention	4.8 ± 1.9	4.9 ± 1.7	0.71
Face-to-face intervention	4.3 ± 1.9	4.4 ± 1.8	0.74
<i>Quality of life - environment</i>			
Mailed intervention	4.9 ± 1.6	4.9 ± 1.6	0.41
Face-to-face intervention	4.4 ± 1.8	4.6 ± 1.8	0.21
<i>Quality of life - activity limitation</i>			
Mailed intervention	5.6 ± 1.3	5.3 ± 1.4	0.63
Face-to-face intervention	4.8 ± 1.6	5.0 ± 1.6	0.93
<i>Quality of life - overall</i>			
Mailed intervention	5.1 ± 1.2	5.0 ± 1.2	0.42
Face-to-face intervention	4.5 ± 1.4	4.7 ± 1.5	0.74
<i>Adherent behaviour</i>			
Mailed intervention	16.3 ± 4.4	16.3 ± 4.4	0.87
Face-to-face intervention	15.5 ± 4.1	17.0 ± 3.7	0.48
<i>Non-adherent behaviour</i>			
Mailed intervention	8.4 ± 2.9	9.6 ± 3.5	0.42
Face-to-face intervention	9.7 ± 2.8	8.2 ± 3.2	0.64
<i>Possession of a written AAP</i>			
Mailed intervention	15/34 (41.1%)	20/60 (33.3%)	0.89
Face-to-face intervention	8/40 (20.0%)	16/48 (33.3%)	< 0.05

There were no significant differences in the post-intervention asthma questionnaire scores or AAP possession between the intervention groups and the control group (Table 34). However, there was a non-significant trend for an increased adherence score and a decreased non-adherence score in the face-to-face intervention group, compared to control.

Table 34. Post-intervention asthma survey results compared to control

Patient-reported outcome	Intervention	Control	<i>P</i>
<i>Asthma control</i>			
Mailed intervention	17.9 ± 4.1	16.3 ± 4.8	0.18
Face-to-face intervention	17.2 ± 4.7	16.3 ± 4.8	0.53
<i>Quality of life - symptoms</i>			
Mailed intervention	4.9 ± 1.1	4.5 ± 1.5	0.16
Face-to-face intervention	4.7 ± 1.4	4.5 ± 1.5	0.65
<i>Quality of life - emotions</i>			
Mailed intervention	4.9 ± 1.7	4.38 ± 1.7	0.28
Face-to-face intervention	4.4 ± 1.8	4.38 ± 1.7	0.97
<i>Quality of life - environment</i>			
Mailed intervention	4.9 ± 1.6	4.8 ± 1.6	0.86
Face-to-face intervention	4.6 ± 1.8	4.8 ± 1.6	0.61
<i>Quality of life - activity limitation</i>			
Mailed intervention	5.3 ± 1.4	4.8 ± 1.8	0.19
Face-to-face intervention	5.0 ± 1.6	4.8 ± 1.8	0.67
<i>Quality of life - overall</i>			
Mailed intervention	5.0 ± 1.2	4.6 ± 1.5	0.24
Face-to-face intervention	4.7 ± 1.5	4.6 ± 1.5	0.88
<i>Adherent behaviour</i>			
Mailed intervention	16.3 ± 4.4	15.4 ± 3.3	0.44
Face-to-face intervention	17.0 ± 3.7	15.4 ± 3.3	0.10
<i>Non-adherent behaviour</i>			
Mailed intervention	9.6 ± 3.5	8.0 ± 2.6	0.07
Face-to-face intervention	8.2 ± 3.2	8.0 ± 2.6	0.86
<i>Possession of a written AAP</i>			
Mailed intervention	20/60 (33.3%)	6/18 (33.3%)	> 0.99
Face-to-face intervention	16/48 (33.3%)	6/18 (33.3%)	> 0.99

3.3.5.3 GP evaluations

Of the 48 GPs who responded to the questionnaire, 29 (60.4%) indicated that they modified, or intended to modify the patient's therapy as a result of this project, and 39 (81.3%) felt that this project appropriately identified their patient as needing a review of their asthma therapy (Table 35).

Table 35. GPs' evaluation of the patient*

Statement	Yes	No
<i>I modified (or intend to modify) this patient's therapy as a result of this project</i>		
Mailed intervention (n = 15)	7 (46.7%)	7 (46.7%)
Face-to-face intervention (n = 19)	13 (68.4%)	5 (26.3%)
Control (n = 14)	9 (64.3%)	5 (35.7%)
Overall (n = 48)	29 (60.4%)	17 (35.4%)
<i>I feel that this project appropriately identified my patient as needing a review of their asthma therapy</i>		
Mailed intervention (n = 15)	11 (73.3%)	3 (20.0%)
Face-to-face intervention (n = 19)	16 (84.2%)	2 (10.5%)
Control (n = 14)	12 (85.7%)	2 (14.3%)
Overall (n = 48)	39 (81.3%)	7 (14.6%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

Table 36 summarises the modifications to patients' asthma therapy as stated by the GPs.

Table 36. Modifications to patient's asthma therapy*

Summarised response	Overall (n = 28)	Mailed intervention (n = 7)	Face-to-face intervention (n = 13)	Control (n = 9)
Added/increased ICS	11 (39.3%)	6 (85.7%)	3 (23.1%)	2 (22.0%)
Education regarding regular use of preventer and use of reliever only when required	8 (28.6%)	0 (0.0%)	5 (38.5%)	4 (44.4%)
Added LABA	2 (7.1%)	0 (0.0%)	0 (0.0%)	2 (22.2%)
Smoking cessation advice	1 (3.6%)	0 (0.0%)	1 (7.7%)	0 (0.0%)
Asthma management plan reviewed	1 (3.6%)	0 (0.0%)	1 (7.7%)	0 (0.0%)
Added long-acting anticholinergic	1 (3.6%)	0 (0.0%)	0 (0.0%)	1 (11.1%)
No elaboration	4 (14.3%)	1 (14.3%)	3 (23.1%)	0 (0.0%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

Of the 7 GPs who did not feel that their patient was appropriately identified as needing a review, 5 (71.4%) provided reasons for this (Table 37).

Table 37. Reasons for GP feeling their patient was not appropriately identified for a review

"[Medication] list [provided by the pharmacy] is not up to date. Patient is on a preventer."
"Patient was advised on last visit by myself that she needed review."
"Bad lungs deteriorating; has lung damage; try to collaborate in the next 2-6 months of which course I should take."
"Having very regular checks with respiratory nurse and spirometry. Current medication all necessary and used in preventer capacity."
"Wife uses patient's reliever at times so dispensing information in this case did not reflect use."

Table 38 displays GPs' perceptions of the intervention. Most GPs agreed or strongly agreed that their patient would benefit from the intervention (32/48, 66.6%). The majority also agreed or strongly agreed that pharmacists are well placed to identify patients who may need a review of their asthma therapy (36/48, 75.0%), that there was an evident need for improved asthma control in the community (37/48, 77.1%) and that this type of program delivered by community pharmacists would improve asthma care in the community if implemented on a larger scale (33/48, 68.8%).

Table 38. GPs' perceptions of the intervention*

Statement	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
<i>I believe that my patient will benefit from this project</i>					
Mailed intervention (n = 15)	3 (20.0%)	6 (40.0%)	4 (26.7%)	0 (0.0%)	1 (6.7%)
Face-to-face intervention (n = 19)	4 (21.1%)	10 (52.6%)	4 (21.1%)	0 (0.0%)	0 (0.0%)
Control (n = 14)	2 (14.3%)	7 (50.0%)	4 (28.6%)	0 (0.0%)	1 (7.1%)
Overall (n = 48)	9 (18.8%)	23 (47.9%)	12 (25.0%)	0 (0.0%)	2 (4.2%)
<i>I believe that pharmacists, utilising dispensing records, are well placed to identify patients who may need a review of their asthma by their doctor</i>					
Mailed intervention (n = 15)	7 (46.7%)	2 (13.3%)	5 (33.3%)	0 (0.0%)	0 (0.0%)
Face-to-face intervention (n = 19)	9 (47.4%)	9 (47.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Control (n = 14)	2 (14.3%)	7 (50.0%)	1 (7.1%)	3 (21.4%)	1 (7.1%)
Overall (n = 48)	13 (27.1%)	23 (47.9%)	6 (12.5%)	3 (6.3%)	1 (2.1%)
<i>I believe that there is an evident need for improved asthma control in the community</i>					
Mailed intervention (n = 15)	5 (33.3%)	8 (53.3%)	0 (0.0%)	1 (6.7%)	0 (0.0%)
Face-to-face intervention (n = 19)	7 (36.8%)	9 (47.4%)	2 (10.5%)	0 (0.0%)	0 (0.0%)
Control (n = 14)	1 (7.1%)	7 (50.0%)	4 (28.6%)	2 (14.3%)	0 (0.0%)
Overall (n = 48)	13 (27.1%)	24 (50.0%)	6 (12.5%)	3 (6.3%)	0 (0.0%)
<i>I believe that this type of program delivered by community pharmacists would be likely to improve asthma control in the community if implemented on a larger scale</i>					
Mailed intervention (n = 15)	2 (13.3%)	7 (46.7%)	3 (20.0%)	2 (13.3%)	0 (0.0%)
Face-to-face intervention (n = 19)	6 (31.6%)	9 (47.4%)	3 (15.8%)	0 (0.0%)	0 (0.0%)
Control (n = 14)	2 (14.3%)	7 (50.0%)	3 (21.4%)	2 (14.3%)	0 (0.0%)
Overall (n = 48)	10 (20.8%)	23 (47.9%)	9 (18.8%)	4 (8.3%)	0 (0.0%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

A number of GPs provided comments about the intervention, pharmacists' involvement and asthma in general (Table 39).

Table 39. GPs' comments regarding the intervention

"Good program."
"Identification ≠ dispensing ≠ consumption."
"[The intervention] needs to be well targeted. Otherwise, [it's] not an efficient use of resources. I'd therefore have some concerns."
"It [the intervention] is a great idea [as] it will sort of what percentage of Australia that do have asthma and what percentage that is and what we can do to help medical and physical."
"Asthma control requires asthma clinics at GP level with regular patient reviews."
"Good idea."
"It [the intervention] has advantages as well as disadvantages."
"People are also panicking over asthma. Parents of children who do not have it [asthma] rush kids to doctors whenever they cough."
"[This project involved] education of the general population rather than spoon-feeding people who do not or will not comply with treatment. That approach wastes resources on patients who will continue non-compliance."
"Here I am again filling in yet another survey along with pharmacy generated question sheets on diabetes, hypertension etc. etc. Overall, together with sheets ++ [sic] from other authorities they are a profound "time waster." As with most GPs I don't even get time for a lunch break."
"Too much interference by pharmacists into many areas of medicine. Stick to selling teddy bears and orthotics."
"Often repeats are made for scripts for Webster packs etc. that are not yet due."

3.3.5.4 Pharmacist satisfaction

Of the 71 pharmacists who participated in the project, 46 (64.8%) completed and returned a satisfaction survey. Table 40 displays pharmacists' perceptions regarding the usefulness and appropriateness of the intervention. The majority of pharmacists agreed or strongly agreed that (i) there is an evident need for improved asthma control in the community (45/46, 97.8%), (ii) the project appropriately identified patients with poorly controlled asthma (37/46, 80.4%) and (iii) the patients identified to be in the intervention group would generally benefit from the project (42/46, 91.3%). The majority of pharmacists were not sure whether mailing information and surveys to patients only is an appropriate way to help them improve their asthma management and control (19/46, 41.3%), while the majority agreed or strongly agreed that handing out information and surveys to patients (face-to-face) only is an appropriate way to help them improve their asthma management and control (34/46, 73.9%).

Table 40. Pharmacists' perceptions regarding usefulness and appropriateness of the intervention*

Statement	Response (n = 46)				
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
I believe that there is an evident need for improved asthma control in the community	24 (52.2%)	21 (45.7%)	0 (0.0%)	1 (2.2%)	0 (0.0%)
I believe that this project appropriately identified patients with poorly controlled asthma	13 (28.3%)	24 (52.2%)	7 (15.2%)	2 (4.3%)	0 (0.0%)
I believe that the patients identified to be in the intervention group will generally benefit from this project	9 (19.6%)	33 (71.7%)	4 (8.7%)	0 (0.0%)	0 (0.0%)
I believe that mailing information and surveys to patients only is an appropriate way to help them improve their asthma management and control	0 (0.0%)	11 (23.9%)	19 (41.3%)	13 (28.3%)	1 (2.2%)
I believe that handing out information and surveys to patients (face-to-face) only is an appropriate way to help them improve their asthma management and control	3 (6.5%)	31 (67.4%)	9 (19.6%)	2 (4.3%)	0 (0.0%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

The majority of pharmacists indicated that they would prefer to perform a face-to-face intervention in usual practice (41/46 [89.1%] preferred face-to-face, 8/46 [8.7%] preferred mailed). Table 41 displays the reasons given for preferring face-to-face or mailed interventions.

Table 41. Pharmacists' reasons for preferring mailed or face-to-face interventions

Reasons for preferring a face-to-face intervention
"Face-to-face intervention [is] probably more effective as some patients won't read information you give them."
"[Provides an opportunity to] get to know the patient."
"Many of the patients identified are elderly and [receiving the] mail out [intervention pack] was a bit confusing [and] overwhelming for some of them. Face-to-face gives you a better chance to explain to the customer what it's all about."
"I think that face-to-face intervention will always be more likely to be accepted by the patient than a mail out approach."
"Mailings may make people feel as though their records are being used incorrectly."
"Better compliance if it's [the intervention] face-to-face."
"Occasional language difficulties mean can only discuss issues face-to-face."
"I think face-to-face interaction from a pharmacist has more impact."
"Face-to-face gives you a chance to elaborate to the patient."
"This [face-to-face intervention] allows the pharmacist to assess the patient's technique, as this is one of the main determining factors of asthma control"
"Face-to-face intervention enables the pharmacist to clarify any issues and concerns regarding asthma management."
"Patients are much more receptive to surveys and counselling/educating when the pharmacist spends time with them and explains the process rather than just mailing something out."
"Face-to-face would be the ideal method because the pharmacist is able to speak with the patient directly and voice any other information or concerns. However, patients may not come in for an extended period of time, which may delay the intervention."
"Obviously face-to-face discussion is more likely to be taken seriously by a patient than a mail out. Also more personal and shows professional care for patient."
"I believe face-to-face to be a better method but I don't think that is appropriate as a single strategy. Mailings as a supplement would be good (occasionally)."
"[I'd prefer to perform the intervention] face-to-face but often they [patients] will not wait (too rushed etc.)"
"Face-to-face contact would give me the opportunity to discuss the intervention with each patient, in a way that would ensure as much as possible that they had a good understanding of the benefits of such an undertaking and the usefulness of taking part."
"I am in a unique position, being a one-man pharmacy and so have personal contact with all my patients. A great trust has developed over the years and face-to-face is the only way to go. A mail out is too impersonal in my situation."
"One-on-one is better."
Reasons for preferring mailed intervention:
"Face-to-face [intervention] may feel defensive."
"Due to a lack of time in day-to-day pharmacy practice mailing the information allows patients to digest the information at their own pace without any pressure. This also allows the patient to go over the information and come back to the pharmacy if they have any questions."
No preference:
"Both options are useful tools. Some patients prefer face-to-face intervention [and] some prefer written information."

Table 42 displays pharmacists' perceptions of the education session, MedeMine-for-Asthma and workflow impact. The majority of pharmacists agreed or strongly agreed that (i) the education session increased their confidence in dealing with asthma management issues (34/46, 73.9%), (ii) the education session increased their confidence in using the MedeMine-for-Asthma program (36/36, 78.3%) and (iii) the MedeMine-for-Asthma program was simple to use (38/46, 82.6%). Most pharmacists agreed or strongly agreed that participation in the project required a minimal amount of their time (42/46, 91.3%). The majority of pharmacists disagreed or strongly disagreed that using the MedeMine-for-Asthma program and implementing the intervention negatively impacted their usual workflow (28/46, 60.9%), while most agreed or strongly agreed that the potential benefits to patients with asthma outweighed the impact on their workflow (42/46, 91.3%).

Table 42. Pharmacists' perceptions of the education session, MedeMine-for-Asthma and workflow impact*

Statement	Response (n = 46)				
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
The education session for pharmacists increased my confidence in dealing with asthma management issues	12 (26.1%)	22 (47.8%)	10 (21.7%)	2 (4.3%)	0 (0.0%)
The education session for pharmacists increased my confidence in using the MedeMine-for-Asthma program	10 (21.7%)	26 (56.5%)	20 (43.5%)	0 (0.0%)	0 (0.0%)
I found the MedeMine-for-Asthma program simple to use	9 (19.6%)	29 (63.0%)	8 (17.4%)	0 (0.0%)	0 (0.0%)
Participation in this project required a minimal amount of my time	7 (15.2%)	35 (76.1%)	4 (8.7%)	0 (0.0%)	0 (0.0%)
Using the MedeMine-for-Asthma program and implementing the intervention negatively impacted my usual workflow	0 (0.0%)	5 (10.9%)	13 (28.3%)	20 (43.5%)	8 (17.4%)
I believe that the potential benefits to patients with asthma outweighed the impact on my workflow	12 (26.1%)	30 (65.2%)	3 (6.5%)	1 (2.2%)	0 (0.0%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

Table 43 displays pharmacists' perceptions regarding general implementation of the intervention. The majority of pharmacists agreed or strongly agreed that (i) they would feel more confident about managing patients with asthma if MedeMine-for-Asthma was routinely available to use (33/46, 71.7%), (ii) pharmacists, utilising dispensing records,

are well placed to identify patients who may need review of their asthma by their doctor (45/46, 97.8%) and (iii) this type of program delivered by community pharmacists will improve asthma control in the community if implemented on a larger scale (46/46, 100.0%).

Table 43. Pharmacists' perceptions regarding general implementation of the intervention*

Statement	Response (n = 46)				
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
I would feel more confident about managing patients with asthma if MedeMine-for-Asthma was routinely available to use	5 (10.9%)	28 (60.9%)	11 (23.9%)	2 (4.3%)	0 (0.0%)
I believe that pharmacists, utilising dispensing records, are well placed to identify patients who may need review of their asthma by their doctor	12 (26.1%)	33 (71.7%)	1 (2.2%)	0 (0.0%)	0 (0.0%)
I believe that this type of program delivered by community pharmacists will improve asthma control in the community if implemented on a larger scale	10 (21.7%)	35 (76.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Would you be willing to participate in other similar projects utilising dispensing records to improve the management of chronic diseases?	Yes: 41 (89.1%)		No: 0 (0.0%)		Unsure: 4 (8.7%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

Twelve pharmacists (26.1%) indicated that they received some form of feedback from patients or GPs regarding the project. Table 44 displays the comments made by pharmacists regarding any feedback given.

Table 44. Pharmacists' comments about patient and GP feedback of the intervention

"Dr [sic] found this a useful tool to speak to patient about their usage, technique about their asthma inhalers."
"Enthusiastic response from local GP for project but disappointing minimal response (as yet?) from patients concerned. Needs my (positive) input regarding response and value of intervention? (as discussed when presenting the surveys originally) Oh well?!"
"Only ONE patient who believed that their asthma was well controlled even though they used the reliever every day."
"Unsure about completing survey as managed by a specialist rather than their GP. Apathy about completing survey."
"Positive."
"Some patients gave positive comments. Others were indifferent and not interested. No GP feedback as yet."
"Drs in area should also receive a package or meeting if on a large scale."
"Only one patient."
"I thought there would be more feedback although we only had small sample. Several commented they had received mail out info [sic]."

A number of pharmacists also provided comments about the intervention (Table 45).

Table 45. Pharmacists' comments about the project

"Idea is good but I think a face-to-face intervention would have gone better with my customers."
"The use of OTC Ventolin [®] should be legislated to be recorded (i.e. the old S3 recordable) so these patients can also be identified."
"Criteria are limiting option as can think of several patients who could improve their asthma management in co-operation with myself and local GP, if they were not excluded by criteria e.g. under 18s and NH [nursing home] residents. 'Some' of those selected are 'lost cases' i.e. lifestyle and attitudes unlikely to improve their response or inclination (e.g. chronic smoker with emphysema who won't use ICS + LABA therapy)."
"This project enables the pharmacist to take more control on management of asthmatics."
"Would be great if the MedeMine program routinely flagged patients for us to 'chat with,' rather than having to remember to try and review their history when dispensing - if on many medications the time to review the history for 3-6 months can be extensive."
"Elderly and non-English speaking patients form a significant proportion of our patient demographic and hence some of our patients identified by this asthma program were ruled out as the material posted would be too difficult to understand - therefore printing the material in another language, e.g. Greek/Italian may be beneficial."
"I've come to believe that just mailing out the 'intervention pack' may limit the usefulness of this project as in my experience face to face counselling only seems to reinforce written material as I think would be the case here. I'd be interested to know which intervention approach (mailed out or face-to-face) was more successful."
"I feel some of my patients should have been included in this project and somehow didn't fit the criteria."
"[There is a] need [for] this research project intervention - to continue, to be self-managed by the pharmacy, [and] to continue reporting on."

3.3.5.5 Patient satisfaction

Table 46 displays patients' perceptions of the intervention. The majority of patients agreed or strongly agreed that they were appropriately identified by their pharmacist as needing a review of my asthma by their doctor (49/108, 45.4%). Most patients also agreed or strongly agreed that (i) use of their asthma reliever reduced over the last year (47/108, 43.5%), (ii) they found the information on asthma management that was sent out with the surveys useful (69/108, 63.9%) and (iii) their asthma control had improved as a result of the project (46/108, 42.6%). The majority of patients agreed or strongly agreed that pharmacists are well placed to identify patients who may need a review of their asthma by their doctors (82/108, 75.9%) and that that this type of program delivered by community pharmacists will improve asthma care in the community if implemented on a larger scale (88/108, 81.5%).

Table 46. Patients' perceptions of the intervention*

Statement	Strongly agree	Agree	Unsure	Disagree	Strongly disagree
<i>I feel that I was appropriately identified by my pharmacist as needing a review of my asthma by my doctor</i>					
Mailed intervention (n = 60)	8 (13.3%)	20 (33.3%)	15 (25.0%)	7 (11.7%)	2 (3.3%)
Face-to-face intervention (n = 48)	6 (12.5%)	15 (31.3%)	16 (33.3%)	4 (8.3%)	2 (4.2%)
Overall (n = 108)	14 (13.0%)	35 (32.4%)	31 (28.7%)	11 (10.2%)	4 (3.7%)
<i>Use of my asthma reliever medication (Ventolin, Airomir, Asmol, Bricanyl) has reduced over the last year</i>					
Mailed intervention (n = 60)	6 (10.0%)	17 (28.3%)	9 (15.0%)	16 (26.7%)	5 (8.3%)
Face-to-face intervention (n = 48)	5 (10.4%)	19 (39.6%)	4 (8.3%)	13 (27.1%)	3 (6.3%)
Overall (n = 108)	11 (10.2%)	36 (33.3%)	13 (12.0%)	29 (26.9%)	8 (7.4%)
<i>I found the information on asthma management that was sent out with the surveys 12 months ago useful</i>					
Mailed intervention (n = 60)	7 (11.7%)	30 (50.0%)	14 (23.3%)	2 (3.3%)	0 (0.0%)
Face-to-face intervention (n = 48)	2 (4.2%)	30 (62.5%)	6 (12.5%)	2 (4.2%)	0 (0.0%)
Overall (n = 108)	9 (8.3%)	60 (55.6%)	20 (18.5%)	3 (2.8%)	0 (0.0%)
<i>I believe that my asthma control has improved as a result of this project</i>					
Mailed intervention (n = 60)	5 (8.3%)	22 (36.7%)	21 (35.0%)	4 (6.7%)	1 (1.7%)
Face-to-face intervention (n = 48)	2 (4.2%)	17 (35.4%)	15 (31.3%)	6 (12.5%)	1 (2.1%)
Overall (n = 108)	7 (6.5%)	39 (36.1%)	36 (33.3%)	10 (9.3%)	2 (1.9%)
<i>I believe that pharmacists are well placed to identify patients who may need a review of their asthma by their doctors</i>					
Mailed intervention (n = 60)	10 (16.7%)	33 (55.0%)	9 (15.0%)	2 (3.3%)	0 (0.0%)
Face-to-face intervention (n = 48)	6 (12.5%)	33 (68.8%)	6 (12.5%)	1 (2.1%)	0 (0.0%)
Overall (n = 108)	16 (14.8%)	66 (61.1%)	15 (13.9%)	3 (2.8%)	0 (0.0%)
<i>I believe that this type of program delivered by community pharmacists will improve asthma care in the community if implemented in a larger program</i>					
Mailed intervention (n = 60)	14 (23.3%)	36 (60.0%)	6 (10.0%)	0 (0.0%)	0 (0.0%)
Face-to-face intervention (n = 48)	12 (25.0%)	26 (54.2%)	7 (14.6%)	0 (0.0%)	0 (0.0%)
Overall (n = 108)	26 (24.1%)	62 (57.4%)	13 (12.0%)	0 (0.0%)	0 (0.0%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses.

Table 47 displays patients' perceptions of asthma care and utilisation of health professionals. The majority of patients agreed or strongly agreed that they are satisfied with the level of asthma care that they usually receive from their doctor (101/108, 93.5%) and from their pharmacist (91/108, 84.3%). While most patients agreed or strongly agreed that they regularly discuss their asthma control and/or management with their doctor (83/108, 76.9%), fewer did so with their pharmacist (42/108, 38.9%).

Table 47. Patients' perceptions of asthma care and utilisation of health professionals*

Statement	Strongly agree	Agree	Unsure	Disagree	Strongly disagree
<i>I am satisfied with the level of asthma care that I usually receive from my doctor</i>					
Mailed intervention (n = 60)	20 (33.3%)	35 (58.3%)	1 (1.7%)	0 (0.0%)	0 (0.0%)
Face-to-face intervention (n = 48)	16 (33.3%)	30 (62.5%)	1 (2.1%)	0 (0.0%)	0 (0.0%)
Overall (n = 108)	36 (33.3%)	65 (60.2%)	2 (1.9%)	0 (0.0%)	0 (0.0%)
<i>I am satisfied with the level of asthma care that I usually receive from my pharmacist</i>					
Mailed intervention (n = 60)	13 (21.7%)	36 (60.0%)	4 (6.7%)	0 (0.0%)	0 (0.0%)
Face-to-face intervention (n = 48)	12 (25.0%)	30 (62.5%)	3 (6.3%)	1 (2.1%)	0 (0.0%)
Overall (n = 108)	25 (23.1%)	66 (61.1%)	7 (6.5%)	1 (0.9%)	0 (0.0%)
<i>I regularly discuss my asthma control and/or management with my doctor</i>					
Mailed intervention (n = 60)	16 (26.7%)	31 (51.7%)	1 (1.7%)	4 (6.7%)	0 (0.0%)
Face-to-face intervention (n = 48)	13 (27.1%)	23 (47.9%)	5 (10.4%)	3 (6.3%)	0 (0.0%)
Overall (n = 108)	29 (26.9%)	54 (50.0%)	6 (5.6%)	7 (6.5%)	0 (0.0%)
<i>I regularly discuss my asthma control and/or management with my pharmacist</i>					
Mailed intervention (n = 60)	6 (10.0%)	17 (28.3%)	9 (15.0%)	13 (21.7%)	5 (8.3%)
Face-to-face intervention (n = 48)	1 (2.1%)	18 (37.5%)	9 (18.8%)	12 (25.0%)	3 (6.3%)
Overall (n = 108)	7 (6.5%)	35 (32.4%)	18 (16.7%)	25 (23.1%)	8 (7.4%)

*Figures represent number (percent) of responses. Percentages may not add up to 100 due to blank responses

A number of patients provided comments about the intervention, pharmacists' involvement in management and their asthma in general (Table 48).

Table 48. Patients' comments regarding the intervention

"I often find doctors and pharmacists have different views on the use of asthma meds [sic]."
"This is a good project. I feel that asthma is like a 'silent killer' in our society. You really don't tell people you have asthma - than you have an attack with them, and I ALWAYS feel embarrassed - because they get so worried - being ignorant - that you will die in front of them."
"How much money are you spending of my taxes?"
"A very good idea - I did a survey test with a department of the Alfred Hospital about 2 years ago. I have other medical problems beside asthma, which makes it a problem to be specific sometimes, i.e. blood pressure, arthritis."
"My doctor selects my medication and dosage, etc. [and] the pharmacist supplies it."
"I find my pharmacist most helpful in many ways."
"[I'm] quite happy with the way I use my medication."
"If chemists were to have on display 'Asthma Action Kits' with solid information, fact sheets, asthma plan sheets and doctor/chemist follow-up plan sheets for free, I feel it would be a good incentive for people with asthma like myself to take one and take a pro-active approach at doing something to encourage asthma management. Thankyou."
"My pharmacist is on top of my asthma control..."
"My [pharmacy name] pharmacist, [pharmacist's name] is a gem, he liaised with my doctor [doctor's name], and I could not ask for any more from my pharmacist."
"My chemist is [pharmacist's name] and is always willing to help."
"I find this [project] a great idea."
"My asthma is well controlled by my preventative meds [sic]. However, any additional information is always a bonus. It is possible to live with asthma IF managed. Keep up the good work."
"I use Ventolin [®] 4 times a day and that seems to control my asthma."

3.4 Discussion

3.4.1 Participants

Approximately 50% of Australian pharmacies use the Fred dispensing system. However, of the pharmacies invited to participate, the proportions who were not users of the Fred dispensing system did not seem to reflect this. In Tasmania, approximately three-quarters of the pharmacies contacted were not using Fred. It should be noted that many pharmacies that were known to use the Fred dispensing system were not invited to participate. This was due to their prior participation in the pilot study,^{5,304} and the possibility that the inclusion of these pharmacies may have skewed the pre-intervention data. In Victoria and South Australia, there was no prior knowledge of which pharmacies did and did not use the Fred dispensing system. Thus, pharmacies were contacted until recruitment targets were reached. In Victoria, less than one-quarter of the pharmacies contacted did not use Fred, while in South Australia, nearly two-thirds

indicated that they did not use Fred. The proportion of pharmacies that used the Fred dispensing system therefore seemed to differ between the states. Approximately one-third of the pharmacists who were contacted used the Fred dispensing system but were not willing to participate. Unfortunately, data exploring the reasons behind their unwillingness to participate was not collected. Follow-up of these pharmacists to determine their perceived barriers to participating in the study may be beneficial to future research.

3.4.2 Uptake of the intervention

Despite efforts to design a pragmatic program and reinforce its use, not all pharmacies followed the study protocol when it came to disseminating the intervention packs. In those pharmacies randomised to perform the face-to-face intervention, approximately 20% of patients did not receive a prescription during the six-week intervention period, thus the pharmacist would not have had the opportunity to offer these patients an intervention. However, even when the opportunity to intervene was taken into account, significantly fewer face-to-face intervention patients were offered an intervention, compared with mailed intervention patients. Several factors may have contributed to pharmacists' willingness to participate and comply with the study methods and protocols. Attendance at the pharmacist education session, time constraints and individual beliefs and perceptions of what constitutes poor asthma control may have influenced the dissemination of intervention packs. It is likely that one of the factors limiting the uptake of the face-to-face intervention was time constraints. Pharmacists who performed the mailed intervention were free to print and compile the intervention packs during quieter times of the day, whereas those who performed the face-to-face intervention were prompted to print and compile the packs as each patient presented to the pharmacy for prescriptions. Although this should have only taken a few minutes, approximately one-third of the electronic prompts were not acted on. This would undoubtedly limit the effectiveness of face-to-face interventions on an intent-to-treat basis.

While there clearly is the potential for community pharmacists to have an impact in improving the management of asthma, such approaches are most likely to be successful if they do not require significant time and additional training on the part of the pharmacist. The need for further research using strategies that are pragmatic in busy

community pharmacies has previously been identified.¹⁰ Disease state management programs may have better uptake and outcomes if they were to utilise information technology, such as MedeMine-for-Asthma, to assist in identification of patients who might be eligible and most likely to benefit from these programs. MedeMine-for-Asthma could assist in the tailoring of information to patients enrolled in disease state management programs and maximise the efficient use of the pharmacist's time.

3.4.3 Patient and GP survey response rates

The average patient response rate of the mailed questionnaires was approximately 13%. This response rate was relatively low, considering that the average patient response rate to postal questionnaires (without reminders or incentives) reported in medical journals is approximately 20-50%.^{350,351}

The personalised letter that was provided with the questionnaires encouraged patients to make an appointment with their GP at their earliest possible convenience. Perceived need for a medical consultation, as well as the cost of a consultation and potential cost of increasing asthma therapy (e.g. the addition of ICS therapy) may have been patient-related barriers to visiting their GP. It is conceivable that some patients did not bother to return the questionnaires if they did not follow the advice of seeking a review of their asthma by their GP. Furthermore, patients' perception of their disease severity (e.g. overestimation of asthma control) and hence their need for an intervention may have limited the motivation to participate.

The average GP response rate of the mailed questionnaires was approximately 5%. The presence of a paired GP questionnaire could not be used as a surrogate measure for whether receiving an intervention letter prompted a visit to the GP. Two unknown factors needed to be taken into consideration when analysing GP questionnaires:

- Patient willingness to visit their GP and give them the questionnaire, and
- GP willingness to complete the questionnaire.

It could not be assumed that the presence or absence of a corresponding GP questionnaire denoted whether or not the patient visited their GP after receiving a letter from their pharmacy. There were five possible scenarios that may have influenced the presence or absence of a corresponding GP questionnaire:

- The patient visited their GP, gave them the questionnaire and it was completed and returned;
- The patient visited their GP, gave them the questionnaire and it was completed but not returned;
- The patient visited their GP, gave them the questionnaire and it was not completed nor returned;
- The patient visited their GP, but did not give them the questionnaire; or
- The patient did not visit their GP.

Lack of time and/or interest on the GPs' part may have influenced their participation. It has previously been reported that the perceived additional workload and paperwork are barriers to implementing interventions designed to improve asthma care.^{275,278,352} Nevertheless, the GP questionnaires provided a useful insight into the management of a number of patients' asthma therapy, as well as an encouraging opinion of the value of this project.

3.4.4 Patient demographics

The mailed intervention, face-to-face intervention and control patients were well matched with respect to demographic measures at baseline. More than half of the patients who responded to the questionnaires were aged 60 years or older. It is possible that this reflected either a higher prevalence of asthma or a greater participation rate in this age group, or both. However, a National Health Survey reported that patients aged 55 years or older actually have a lower prevalence of asthma, with patients aged between 15 and 35 years having the highest prevalence.³¹ Conversely, it has been reported that older patients have higher participation rates in asthma interventions than younger patients.^{353,354}

Similarly, females accounted for more than half of the patients who responded to the questionnaires. It is likely that this reflected a higher prevalence of asthma among females,³¹ and a higher participation rate,³⁵⁵ both of which have been reported previously.

3.4.5 Outcome measures

3.4.5.1 Dispensing data

The intervention resulted in significant improvements in the P : R ratio in both intervention groups and the control group. Using the treatment received method of analysis, the magnitude of improvement in the face-to-face intervention group was greater than that in the mailed intervention group, which was greater than that in the control group. The improved effectiveness of the face-to-face intervention may have been due to two key factors: (i) the personalised delivery by a pharmacist, and (ii) the patients' perception of their asthma severity and control at the time of the intervention. The face-to-face intervention would undoubtedly be expected to have a greater impact on a patient-by-patient basis, due to the personalised method of delivery by their community pharmacist, someone they presumably know and trust. The pharmacist had the option of delivering tailored advice to each patient, and the patient had the opportunity to raise any queries or concerns they may have had. Furthermore, the intervention was delivered at a time the patient had presenting to the pharmacy for the collection of their medications (including, quite possibly, their asthma medication), so it is likely that their overall health and asthma was at the front of their minds at the time. Moreover, if the patient had presented to the pharmacy specifically to collect a reliever inhaler, their perception of their asthma severity may have been worse than if they had received the intervention pack in the mail on any other day. A worse perception of one's asthma severity may have increased the acceptance of the intervention by such patients, and improved adherence to the recommendations made.

Unfortunately, the seemingly improved effectiveness of the face-to-face intervention compared to the mailed intervention was offset by its decreased delivery by pharmacists. Taking the decreased delivery of the face-to-face intervention into account, the overall magnitude of improvement in the mailed intervention group was greater than that in the face-to-face intervention group. It seems that time constraints in busy pharmacies may restrict the uptake and effectiveness of face-to-face interventions in the 'real world' setting. Hence, perhaps both intervention options should be made available, for the pharmacist to deliver at their own discretion.

It should be noted that the P : R ratio and reliever usage also significantly improved in the control group (albeit, to a lesser degree than in the intervention groups). Changes in

the control group may have also reflected a change in pharmacists' behaviour towards all patients with asthma presenting to the pharmacy, due to a heightened awareness of asthma management issues arising from participation in the project (including attendance at the education sessions). This effect, known as the Hawthorne Effect, stipulates that the mere awareness of being under observation can alter the way in which a person behaves. If there is a demonstrable benefit from participating in clinical research, for whatever reason, then this has implications for good clinical practice and for improving care. The Hawthorne Effect is a component of the non-specific effects of trial participation, but is not controlled for by usual controlled trial designs.³⁵⁶

Another important point to note is that most of the significant differences arose from within-group comparisons rather than between-group comparisons. It was unfortunate that there were not enough differences between the groups after the intervention to detect any statistical significance. However, post hoc between-group analysis of the reduction in reliever usage demonstrated trends of borderline significance for both intervention groups to have a great reduction in reliever usage after the intervention than the control.

Despite the fact that the P : R ratio was the primary outcome measure used in this project, further analyses were necessary in order to determine whether the increase in the P : R ratio resulted from an increased preventer usage or a decreased reliever usage, before any conclusions could be drawn. Further analysis found that the increased P : R ratio was largely due to a reduction in the average daily use of reliever medication (of borderline statistical significance). A number of international studies have demonstrated improved asthma outcomes with decreased reliance on reliever medications.^{129,316-319} Additionally, a number of studies have implicated regular and perhaps excessive use of SABA in asthma deaths and near-death emergencies⁸⁹⁻⁹⁵ and worse clinical outcomes.⁹⁶⁻⁹⁸ The concerns about adverse outcomes with frequent and regular SABA use are likely to have mainly been related to suboptimal use of ICS in patients whose asthma was inadequately controlled and treated.⁸⁵

The average salbutamol-equivalent daily usage of SABA before the intervention was 655.7 µg, which equates to 6-7 puffs per day. This range of daily SABA consumption was well above what is recommended by the National Asthma Council and Asthma Foundations Australia, who state that usage of reliever medication on three or more

occasions per week is indicative of suboptimal asthma control.^{59,328} According to Australian asthma management guidelines, and assuming all dispensed medication had been consumed, patients using this quantity of reliever medication should be classed as having poor asthma control, and should have been receiving regular ICS therapy.⁵⁹ Therefore, the algorithm used by the MedeMine-for-Asthma program seemed to appropriately identify patients who were likely to have poor asthma control. The identical medians in daily pre-intervention SABA usage between the three groups in the intention-to-treat analyses demonstrated the effectiveness of the randomisation process included in the program's identification algorithm. By ranking all identified patients by their SABA usage and then randomly assigning them to the intervention or control group, the program ensured that the groups were well-matched at baseline.

It was assumed that the dispensed quantity of reliever medication equated with actual medication consumption, but factors such as storing relievers in different sites and misplacing medication could complicate the picture. These factors may have resulted in reduced measurement precision of medication usage, but are unlikely to have introduced systematic bias, as they existed both before and after the intervention and in both intervention and control groups. It is also possible that non-prescription supply of relievers, which is not always recorded in the dispensing software, resulted in underestimation of reliever medication usage. Underestimation may also have arisen from the assumption that asthma medications were not being dispensed at other pharmacies. However, the same level of underestimation would have applied to both groups and in both the pre- and post-intervention periods.

While it was encouraging to see a sustained improvement in the P : R ratio and decrease in reliever usage, it was somewhat disappointing that the usage of ICS did not significantly increase as a result of the intervention. Reasons for no change in preventer use could be because people used them better and/or people started using the preventer that had been dispensed previously, which would not be picked up in increased dispensings. There may be barriers to ICS use, which need to be addressed in future intervention programs.

3.4.5.2 Patient-reported outcomes

It was somewhat disappointing that there were no significant improvements in patient-reported asthma control, quality of life or medication adherence behaviour after the

intervention. We have previously demonstrated that a mailed intervention significantly improved patient-reported asthma control and quality of life six months after the intervention.³⁰⁴ Therefore, one of the reasons for no improvement in this study may have been due to the delayed follow-up (12 months) after the intervention. Perhaps the improvements in patient-reported outcomes previously demonstrated would not be sustainable over a 12-month period. It should be mentioned that the reason for using a 12-month follow-up in this study was to ensure that seasonal variations in dispensing pattern and asthma control did not influence the results. Another reason for the lack of significant improvement in most patient-reported outcomes may have been due to the low return rate of the patient questionnaires. Therefore, small sample sizes may have prevented any significant differences from being detected.

There was, however, a non-significant trend for improved asthma control after the face-to-face intervention, but not after the mailed intervention. This adds weight to the treatment-received analysis of dispensing data, which suggested that the face-to-face intervention was more effective than the mailed intervention among those patients who actually received the intervention. Due to the low questionnaire response rate, it was not known what total proportion of patients sought a review of their asthma therapy as a result of receiving an intervention pack. The improvements in asthma control therefore may have been GP-initiated, via prescribing additional preventer therapy, or patient-related, via an increased awareness of their condition after being alerted to their high reliever usage.

There was also a significant increase in the proportion of patients who possessed written AAPs after the face-to-face intervention, but not after the mailed intervention. Providing an individualised written AAP is a high-profile part of Steps 5 and 6 of the Australian Asthma Management Plan: “develop an action plan” and “educate and review regularly.”³⁵⁷ The use of a written AAP in conjunction with training in self-management and regular medical review has been shown to reduce asthma-related unscheduled visits to the doctor, days off work or school and risk of death, as well as improved asthma symptoms and quality of life.^{74,85}

It has previously been reported that it was not possible to achieve AAP ownership in 100% of people with asthma, despite referrals for this purpose,³⁰⁰ and it has been suggested that a better collaborative inter-professional network needs to be established

so that all healthcare professionals support AAP ownership.³⁰¹ Perhaps in future, asthma interventions could focus more on the development of a written AAP, and reinforcement of the plan by community pharmacists, to tie in more closely with the current objectives of the Asthma Foundations, although the patient- and GP-related barriers to the implementation of AAPs, as discussed earlier in this thesis, would need to be addressed.

3.4.5.3 GP evaluations

There were two sets of GP surveys; those from the intervention patients sent out at the time of the intervention, and those from the control patients, sent out 12 months after the original intervention. The 'intervention' GP surveys supported intervention outcomes, whereas the 'control' GP surveys simply provided further insight into GPs' perception of asthma control and asthma therapy.

While the low return rate to the GP survey limits the generalisation of these results, the GP responses provided a useful insight into the management of a number of patients' asthma therapy, as well as an encouraging opinion of the value of this project. More than half of GPs who returned questionnaires indicated that they modified or intended to modify their patient's asthma therapy. The modifications, as stated by the GP, were predominately the addition of ICS therapy. It has already been shown in a number of studies that regular use of ICS can reduce asthma symptoms,^{171,358} prevent exacerbations and hospitalisations,^{171,359} and reduce asthma mortality.¹²¹ Other modifications to patients' therapy included simple education regarding the regular use of ICS and over-reliance on relievers, changes to existing ICS therapy, the addition of a LABA or anticholinergic therapy, review of asthma management plan and smoking cessation advice.

More than 80% of GPs agreed that their patient was appropriately identified for a review of their asthma therapy and nearly two-thirds agreed or strongly agreed that their patient would benefit from this project. This was particularly encouraging, as it added strength to the algorithm used by the MedeMine-for-Asthma program in appropriately identifying patients who are in need for improved asthma management.

The second part of the GP questionnaire assessed the GPs' opinions on the usefulness of this project and of projects such as this one. Specifically, it assessed whether the GP

agreed that (i) pharmacists are well placed to identify patients who may need review of their asthma therapy, (ii) there is an evident need for improved asthma management in the community, and (iii) this type of program delivered by community pharmacists would be likely to improve asthma care in the community if implemented on a larger scale. Importantly, the majority of GPs agreed with these statements. Indeed, it has been reported that one of the priorities GPs nominate for achieving best outcomes for asthma care is facilitating regular patient review.²⁷⁵ Unfortunately, there still seems to be some negative attitudes towards pharmacists and their role in healthcare. This was classically illustrated by a quote made by one GP:

“Too much interference by pharmacists into many areas of medicine. Stick to selling teddy bears and orthotics.”

One key way to overcome this type of attitude is for pharmacists to continue to perform interventions, with effective collaborations with GPs, with the ultimate aim of improving patient care. More interventions such as this one can demonstrate that pharmacists can effectively use skills and resources to improve health outcomes.

It has been well documented that a potential patient barrier to optimal asthma management and control is the patients' underestimation of their disease severity.^{51,52,281} The 2005 International Control of Asthma Symptoms (ICAS) survey of patients and GPs found high levels of concerns amongst GPs that patients accept their symptoms as normal, and frustration that their patients were not more forthcoming about their symptoms.²⁸⁴ It seemed that too many patients have symptoms that they accept as being part of their condition and many rely heavily on their rescue medication. This intervention included a personalised letter to patients who were 'high-users' of reliever medications, suggesting that this may indicate that their asthma was not under control. By bringing their attention to the fact that their asthma could be better controlled and suggesting that they see their GP for a review of their asthma, the project attempted to bridge the gap between patients and GPs to improve asthma management.

3.4.5.4 Pharmacist satisfaction

The pharmacist satisfaction questionnaire was a useful insight into the perception of the project's methods, usefulness and relevance. More than 80% of pharmacists agreed that the project appropriately identified patients with poorly controlled asthma, and more

than 90% agreed that the patients identified to be in the intervention group would benefit from the project. Again, this added strength to the algorithm used by the MedeMine-for-Asthma program in appropriately identifying patients who were in need of education for improved asthma management. Interestingly, the majority of pharmacists were not sure whether mailing information and surveys to patients only is an appropriate way to help them improve their asthma management and control, while more than 70% agreed that handing out information and surveys to patients (face-to-face) only is an appropriate way to help them improve their asthma management and control. When asked which type of intervention they would prefer to perform in usual practice, nearly 90% indicated that they would prefer to perform the face-to-face intervention. This was despite the fact that significantly fewer face-to-face intervention patients were offered an intervention, compared with mailed intervention patients. This suggests that the pharmacists' personal beliefs about the nature of the intervention did not affect the uptake. Other factors such as time constraints may have limited the uptake of the face-to-face intervention. Indeed, one pharmacist also made the comment that patients are often too rushed to receive an intervention in the pharmacy. Comments made by pharmacists regarding their preference for intervention type suggested that the main reasons for preferring to perform the face-to-face intervention were the personalisation and delivery of professional care and increased acceptance by patients.

3.4.5.5 Patient satisfaction

The patient satisfaction survey provided a useful insight into perceptions of asthma medication, the need for an intervention to improve asthma management, and the perceptions towards and utilisation of healthcare professionals. It was very encouraging that most patients agreed that they were appropriately identified by their pharmacist as needing a review of their asthma by their doctor, and that their asthma control had improved as a result of the intervention. Most patients also seemed to recognise the potential role that pharmacists can play in improving asthma management, with three-quarters of patients agreeing that pharmacists are well placed to identify patients who may need a review of their asthma by their doctors, and more than 80% agreeing that this type of program delivered by community pharmacists would improve asthma care in the community if implemented on a larger scale.

More than 80% of patients indicated that they were satisfied with the level of asthma care that they usually receive from their doctor and from their pharmacist. It was surprising and somewhat disappointing that while three-quarters of patients agreed that they regularly discuss their asthma control and/or management with their doctor, only one-third did so with their pharmacist. Nevertheless, many positive comments were made about pharmacists, and the fact they are very willing to help patients with their asthma.

3.5 Conclusions

Community pharmacy dispensing records can be effectively utilised, with appropriately designed data mining software, to identify patients with suboptimal asthma management, who can then be referred to their GP for review. The face-to-face intervention improved asthma management to a greater degree than the mailed intervention, but only among those who received the intervention. Time constraints in busy pharmacies may limit the uptake and effectiveness of face-to-face interventions in the 'real world' setting. Pharmacists should have both mailed and face-to-face intervention options available to ensure maximum uptake and effectiveness of the interventions.

Using the MedeMine-for-Asthma program, approximately 1500 patients were identified from 71 pharmacies as having suboptimal asthma management. If the program were to be made compatible with all dispensing systems, and the intervention was implemented on a national scale, more than 100,000 patients could be readily identified from approximately 5,000 pharmacies. The MedeMine-for-Asthma program was shown to be pragmatic in its use, and with minor modifications, it could potentially be utilised to perform interventions to improve the management of other chronic conditions.

PART THREE:

MEDICATION PERSISTENCE IN COPD

CHAPTER FOUR: INTRODUCTION

4.1 Pathophysiology of COPD

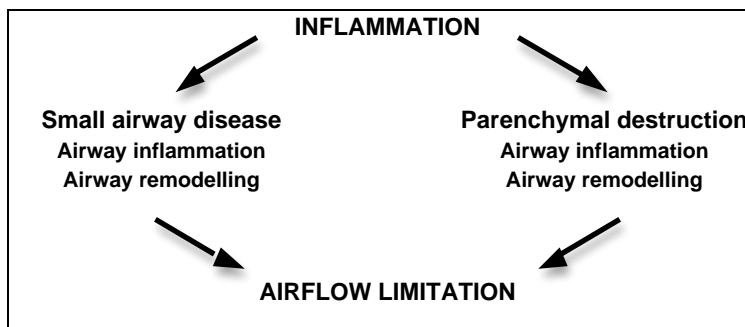
Chronic obstructive pulmonary disease (COPD) is a disease state characterised by a progressive limitation of airflow in the lungs which, unlike asthma, is not fully reversible by medication.³⁶⁰ the characteristic symptoms of COPD are chronic and progressive dyspnoea, cough and sputum production. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) definition for COPD is:

“COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.”³⁶⁰

It is important to note that the terms ‘chronic bronchitis’ and ‘emphysema’ are no longer included in the formal definition of COPD, although they are still used clinically.³⁶⁰ Emphysema is a pathologic term used to describe destruction of the alveolar-capillary membrane, and chronic bronchitis is a clinical term used to describe the presence of cough or sputum production for at least a three-month duration during two consecutive years.³⁶¹

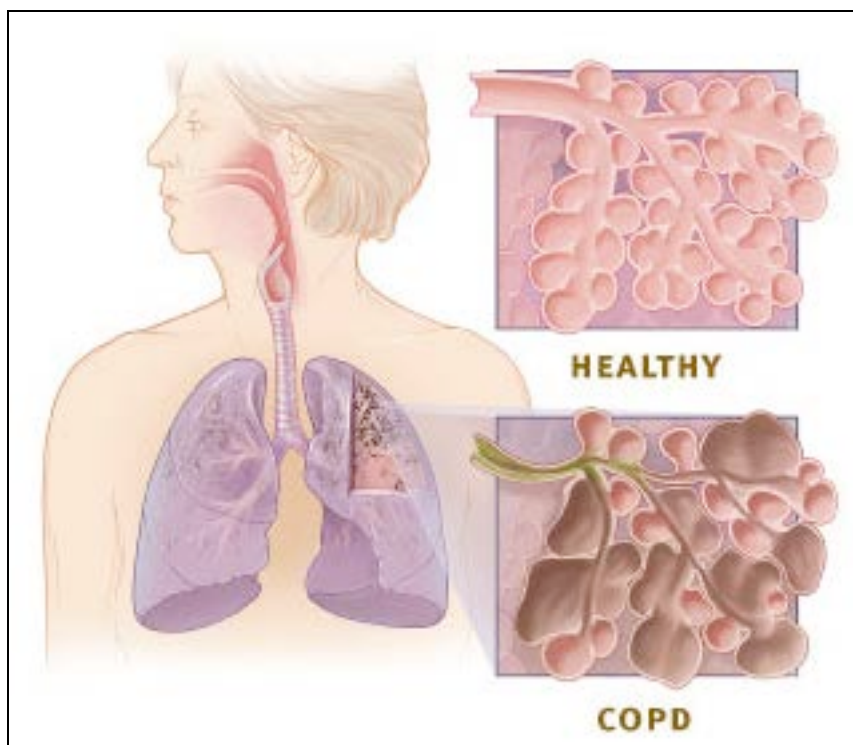
The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which varies between patients (Figure 26).³⁶⁰

Figure 26. Mechanisms of underlying airflow limitation in COPD³⁶⁰



Prolonged exposure to toxic gases or particles causes chronic inflammation, which results in structural changes and narrowing of the small airways (Figure 27).³⁶² Destruction of the lung parenchyma, also by inflammatory processes, leads to the loss of alveolar attachments to the small airways and decreased lung elastic recoil.³⁶³⁻³⁶⁵ These changes result in a prolonged time constant for lung emptying and decreases expiratory airflow.³⁶⁶

Figure 27. Illustrative representation of the pathophysiological changes in COPD³⁶⁷



Airflow limitation, measured by reduced FEV₁, progresses slowly over several decades, so that most patients with symptomatic COPD are in late middle age or are elderly.³⁶⁸ Spirometry is essential for diagnosis and provides a useful description of the severity and pathological changes in COPD (Table 49).³⁶⁰

Table 49. Spirometric classification of COPD severity³⁶⁹

COPD classification	Post-bronchodilator FEV ₁
Stage I: mild	FEV ₁ /FVC* ratio < 0.70, FEV ₁ ≥ 80% predicted
Stage II: moderate	FEV ₁ /FVC ratio < 0.70, 50% ≤ FEV ₁ < 80% predicted
Stage III: severe	FEV ₁ /FVC ratio < 0.70, 30% ≤ FEV ₁ < 50% predicted
Stage IV: very severe	FEV ₁ /FVC ratio < 0.70, FEV ₁ < 30% predicted <i>or</i> < 50% predicted plus chronic respiratory failure [†]

*FVC = Forced vital capacity. [†]Respiratory failure: arterial partial pressure of oxygen < 60 mm Hg with or without arterial partial pressure of CO₂ > 50 mm Hg while breathing air at sea level.

The natural course of COPD is complicated by the development of extra-pulmonary effects, including systemic inflammation, weight loss, skeletal muscle dysfunction, cardiovascular disease, anxiety, depression and osteoporosis (Table 50).³⁷⁰ The high burden of COPD resulting from respiratory symptoms is further contributed to by these systemic effects, leading to a pronounced deterioration of health status, a diminished QOL and increased mortality.³⁷¹ While the relationships between the pulmonary and extra-pulmonary effects of COPD are not fully understood, local and systemic inflammation, oxidative stress and disturbances in neuro-hormonal states are some of the likely mechanisms.³⁷² The involvement of common susceptible genes or risk factors is also possible.

Table 50. Systemic effects of COPD³⁷⁰

Type of effects	Examples of effects
Systemic inflammation	Oxidative stress ^{373,374}
	Activated inflammatory cells ^{375,376}
	Increased plasma levels of cytokines and acute phase proteins ^{377,378}
Nutritional abnormalities and weight loss	Increased resting energy expenditure ³⁷⁹
	Abnormal body composition ³⁸⁰
	Abnormal amino acid metabolism ³⁸¹
Skeletal muscle dysfunction	Loss of muscle mass
	Abnormal muscle structure/function ^{382,383}
	Exercise limitation ³⁸⁴
Other potential systemic effects	Cardiovascular effects (e.g. ischemic heart disease) ³⁸⁵
	Nervous system effects (e.g. anxiety and depression) ³⁸⁶
	Osteoskeletal effects (e.g. osteoporosis) ³⁸⁷

COPD is a heterogeneous disease process that varies greatly from person to person with respect to lung pathology, natural history of disease and systemic effects and co-morbidities.^{388,389} The risk for COPD is related to an interaction between genetic factors and many different environmental exposures.³⁹⁰ It appears that an enhanced or abnormal inflammatory response to inhaled particles or gases, beyond the normal protective inflammatory response in the lungs, is a characteristic feature of COPD and has the potential to produce lung injury.³⁹¹ Cigarette smoking is by far the most commonly encountered risk factor for COPD.³⁹⁰ The population-attributable risk of smoking (current smoking and ex-smoking) for COPD is reportedly up to 78%.³⁹² This population-attributable risk identifies that at least 22% of COPD still needs to be explained by other genetic and environmental risk factors. However, due to complex relationships between the known risk factors for COPD, individuals with similar smoking and exposure histories can vary a great deal in their predisposition to the disease, severity of their disease and response to intervention. Most of the evidence concerning risk factors for COPD (Table 51) comes from cross-sectional epidemiological studies that identify associations rather than cause-and-effect relationships.

Table 51. Risk factors for COPD

Type of risk factor	Examples
Exposure to particles	Tobacco smoke ³⁹³⁻³⁹⁵
	Occupational dusts (organic and inorganic) ³⁹⁶
	Indoor air pollution from heating and cooking with biomass ^{397,398}
	Outdoor air pollution ^{398,399}
Genetic	Hereditary deficiency of the serine protease inhibitor alpha-1 antitrypsin ⁴⁰⁰⁻⁴⁰³
Lung growth and development	Low birth weight ^{404,405}
	Reduced maximal attained lung function ⁴⁰⁶
Infections	Exposure to respiratory infections in childhood ^{405,407}
Ageing	Age over 40 years ^{393,394}
Gender	Prevalence of COPD higher in males ^{393,408}
	Females may be more susceptible to the effects of tobacco smoke ⁴⁰⁹⁻⁴¹¹
Socioeconomic status	Low socioeconomic status and/or factors relating to low socioeconomic status (e.g. poor nutrition and high exposure to particles) ^{412,413}
Asthma	There is a large overlap between people who have a clinical diagnosis of COPD and asthma, and people with asthma can lose lung function more rapidly than people without asthma ⁴¹⁴⁻⁴¹⁶

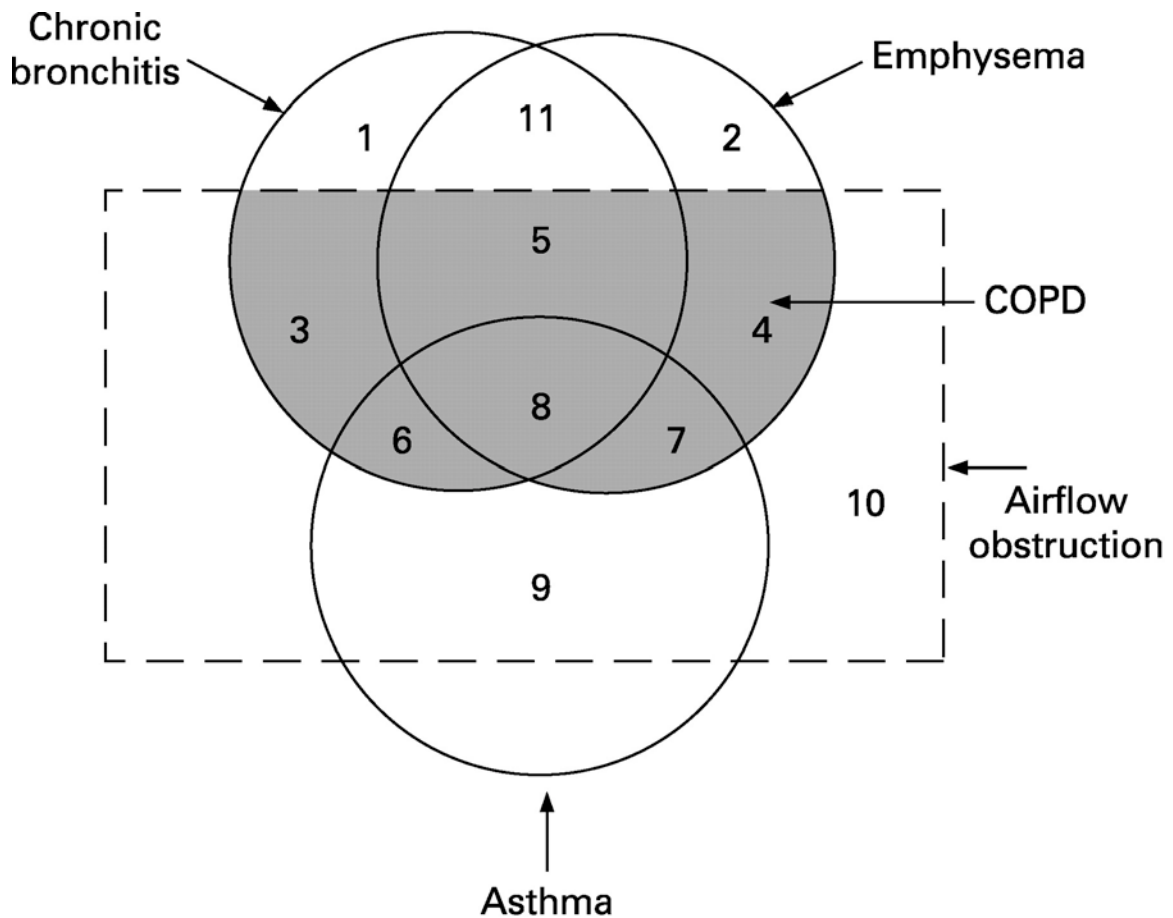
4.2 Overlap of COPD and asthma

Asthma and COPD have important similarities and differences. Both are chronic inflammatory diseases that involve the small airways and cause airflow limitation, both result from gene-environment interactions and both are usually characterised by mucous and bronchoconstriction. Differentiation between asthma and COPD is important because the prognosis, treatment goals and several aspects of the guideline-recommended management strategies differ for these diseases.^{16,360} Once COPD is established, the only interventions that influence life expectancy are smoking cessation and oxygen therapy.³⁶⁰ By contrast, most patients with asthma have a normal life expectancy if they maintain regular preventive anti-inflammatory medication.¹⁶

Although overlaps exist in the disease characteristics of asthma and COPD, careful history, physical examination and lung function testing often reveal information that facilitates distinction between these diseases, allowing better tailoring of therapy. A misdiagnosis of COPD or asthma may lead to inadequate management of patients and to escalating healthcare costs. An early and accurate diagnosis can help ensure optimal and cost-effective management of patient care.

Until recently, the presence or absence of reversibility of airflow obstruction was thought to be the major distinction between asthma and COPD, with reversibility being the hallmark of asthma and mainly irreversibility being the hallmark of COPD.⁴¹⁷ In reality asthma and COPD are not single entities; each has a spectrum of reversibility and there is ‘overlap,’ most likely associated with the varying extent and the ‘mix’ of both structural and inflammatory changes, and the predominant anatomic site within the lung at which these occur.⁴¹⁸ Individual patients commonly share the traits of different obstructive lung diseases.^{419,420} A graphical representation of this relationship was first presented as the non-proportional Venn diagram of chronic airflow obstruction (Figure 28).

Figure 28. Non-proportional Venn diagram of COPD⁴²¹



The subsets comprising COPD are shaded. Subset areas are not proportional to the actual relative subset sizes. Asthma is by definition associated with reversible airflow obstruction although, in variant asthma, special manoeuvres may be necessary to make the obstruction evident. Patients with asthma whose airflow obstruction is completely reversible (subset 9) are not considered to have COPD. Because in many cases it is virtually impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from persons with chronic bronchitis and emphysema who have partially reversible airflow obstruction with airway hyperreactivity, patients with unremitting asthma are classified as having COPD (subsets 6, 7 and 8). Chronic bronchitis and emphysema with airflow obstruction usually occur together (subset 5), and some patients may have asthma associated with these two disorders (subset 8). Individuals with asthma who have been exposed to chronic irritation, as from cigarette smoke, may develop chronic productive cough, which is a feature of chronic bronchitis (subset 6). Persons with chronic bronchitis and/or emphysema without airflow obstruction (subsets 1, 2 and 11) are not classified as having COPD. Patients with airway obstruction due to diseases with known aetiology or specific pathology such as cystic fibrosis or obliterative bronchiolitis (subset 10) are not included in this definition.

It is well established that airway remodelling can occur in long-standing, poorly treated asthma and results in partially reversible airflow obstruction.^{422,423} Therefore, in many patients with long-standing asthma there is a component of irreversible airflow obstruction with reduced lung function and incomplete response to a short-acting bronchodilator or to an oral or inhaled corticosteroid. This makes the diagnosis of obstructive lung disease somewhat challenging in older adults. However, despite similar

airflow obstruction, elderly patients with asthma have distinct characteristics compared to patients with COPD.⁴²⁴ Long-term asthma has also been associated with an accelerated decline of FEV₁.⁴¹⁴ If patients with asthma sometimes show COPD-related phenotypes such as irreversible airflow obstruction and lung function decline, patients with COPD may exhibit airflow functional signs that are characteristic of asthma. Indeed, partial response to a bronchodilator is a common feature in patients with COPD, with almost 50% of patients showing significant improvement in FEV₁ after a bronchodilator.^{425,426} Interestingly, among patients with COPD, reversibility after bronchodilators appears to be associated with other asthma-related phenotypes, such as bronchial hyper-responsiveness.⁴²⁷

Just how commonly does asthma and COPD co-exist? A number of studies have attempted to answer this question by analysing health surveys, Medicaid data, general practice databases or by classifying patients according to respiratory characteristics derived from international consensus guidelines. Amongst patients with obstructive lung disease, the reported overlap of asthma and COPD ranges from 17-55% of patients.^{419,428,429} Variations in the rates of overlap seem to stem from different methods of classification and differing study populations. Furthermore, diagnostic confusion between asthma and COPD appears commonly in the primary care setting.⁴³⁰ The proportion of patients with mixed disease seems to increase with age,⁴¹⁹ and the burden of the concomitant diseases is reportedly much higher than the combined burden of both individually.⁴²⁹

Asthma and COPD tend to be treated with the same medications, with variations on emphasis (Table 52). Asthma is optimally treated with regular anti-inflammatory medications (preferably ICS), and short-acting bronchodilators are used when needed.¹⁶ COPD is usually treated with long-acting bronchodilators, which provide symptomatic benefits, and ICS to reduce the frequency of exacerbations.³⁶⁰ Whilst chronic inflammation underlies both asthma and COPD, the nature of the inflammation differs, as does the response to anti-inflammatory medications.^{431,432}

Table 52. Major differences between asthma and COPD management in adults⁵⁹

Asthma	COPD
Regular ICS treatment is recommended for patients of all ages with persistent asthma.	ICS are generally reserved for patients with severe disease and frequent exacerbations, or those who have shown improvement with ICS therapy
Inhaled anticholinergic agents (e.g. tiotropium, ipratropium) are not commonly used.	Inhaled anticholinergic agents improves dyspnoea, exacerbation rates, exercise capacity and health status
Antibiotics are rarely indicated to manage exacerbations	The use of antibiotics is often appropriate in the management of exacerbations

Differences in these diseases can be found in the goals of treatment. In asthma, treatment should be aimed at primarily achieving normal or near-normal lung function and preventing symptoms, which allows patients to live a relatively normal life.¹⁶ In COPD, the goal of therapy is to reduce the progressive nature of the disease with a focus on reducing symptoms and exacerbations while improving physical functioning and quality of life.³⁶⁰ Basically, the pharmacological treatment of asthma is driven by the need to suppress the chronic inflammation, whereas in COPD, pharmacological treatment is driven by the need to reduce symptoms.⁴¹⁷

While consensus-based management guidelines for asthma and COPD acknowledge that the two diseases may co-exist, succinct treatment recommendations for mixed cases are lacking. Management should therefore be tailored to the individual's symptoms, physical functioning and frequency of exacerbations. Future research is required to determine whether patients with coexisting signs of asthma and COPD may benefit from management strategies that are based on multiple functional, morphologic and immunologic assessments rather than a categorisation into rigid diagnostic labels of either asthma or COPD.⁴³³

Tailoring treatment to individual patients and assessing its benefits carefully should maximise quality of life, reduce adverse effects of medication, optimise physical function and better prepare patients for exacerbations.⁴³⁴ Adapting management strategies to meet the individual patient's needs should be the overriding consideration in achieving better outcomes for patients with obstructive airways disease.

4.3 Burden of COPD

COPD is an important cause of morbidity, mortality and healthcare costs worldwide. Estimates from the World Health Organisation's Global Burden of Disease and Risk Factors project estimated that COPD was the fifth leading cause of death worldwide in 2001⁴³⁵ and will be the third leading cause by 2020.⁴³⁶ The World Health Organisation estimates that more than 2.5 million people die of COPD each year, which is about the same mortality rate as HIV/AIDS. Many sources of variation can affect estimates of COPD prevalence, including sampling methods, response rates and quality of spirometry.³⁶⁰ Despite these complexities, data is emerging that enable some conclusions to be drawn regarding COPD prevalence. The Burden of Obstructive Lung Disease (BOLD) initiative developed standardised materials for estimating COPD prevalence using post-bronchodilator spirometry testing plus questionnaires about respiratory symptoms, health status and exposure to COPD risk factors.⁴³⁷ It was estimated the worldwide prevalence of stage II or higher COPD for people aged 40 years or older to be 10.1% overall, 11.8% for men and 8.5% for women.^{393,394} Furthermore, there is evidence that the prevalence of COPD (stage I) is appreciably higher in smokers and ex-smokers than in non-smokers, in those over 40 years than those under 40, and in men than in women.⁴³⁸

COPD is currently the tenth leading cause of disease burden in the world, causing approximately 2% of the entire global burden of disease.⁴³⁹ It is expected that COPD will move up to the fifth leading cause of disease burden by 2020,⁴⁴⁰ unless action is taken to control leading risk factors for the disease.

COPD is also a significant health problem in Australia. Estimates from the 2004-05 National Health Survey indicated that about 2.9% of the Australian population had emphysema or bronchitis, with the prevalence rising to 7.8% by the age of 75 years and over (Figure 29).⁸

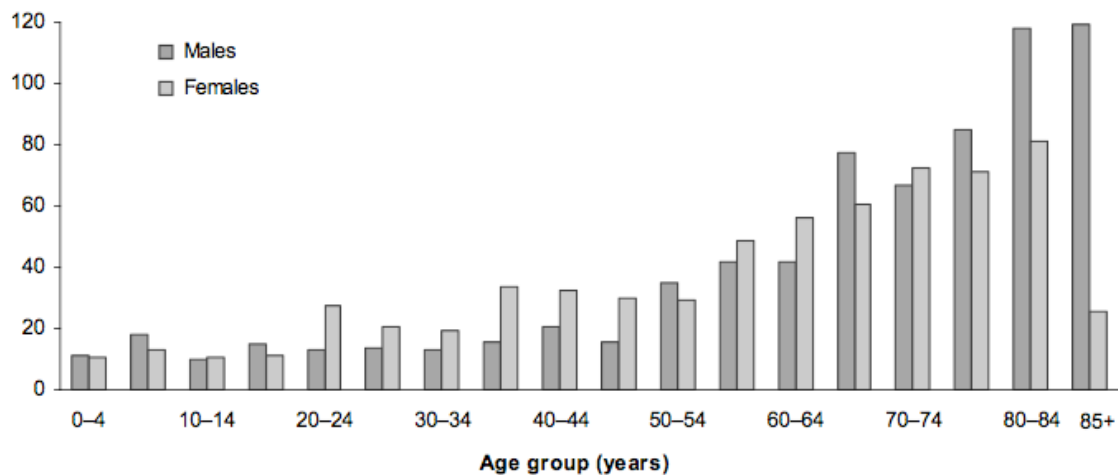
Figure 29. Number with emphysema/bronchitis per 1,000 population, Australia 2004-05⁸

Figure 29 displays a higher than expected prevalence in people ages less than 40 years, possibly due to the reliance on self-report of the broadly defined conditions of chronic bronchitis and emphysema. More recent estimates from the Australian part of the BOLD population-based prevalence study suggest a prevalence of 9.3% in those aged 40 years or older.⁴³⁷

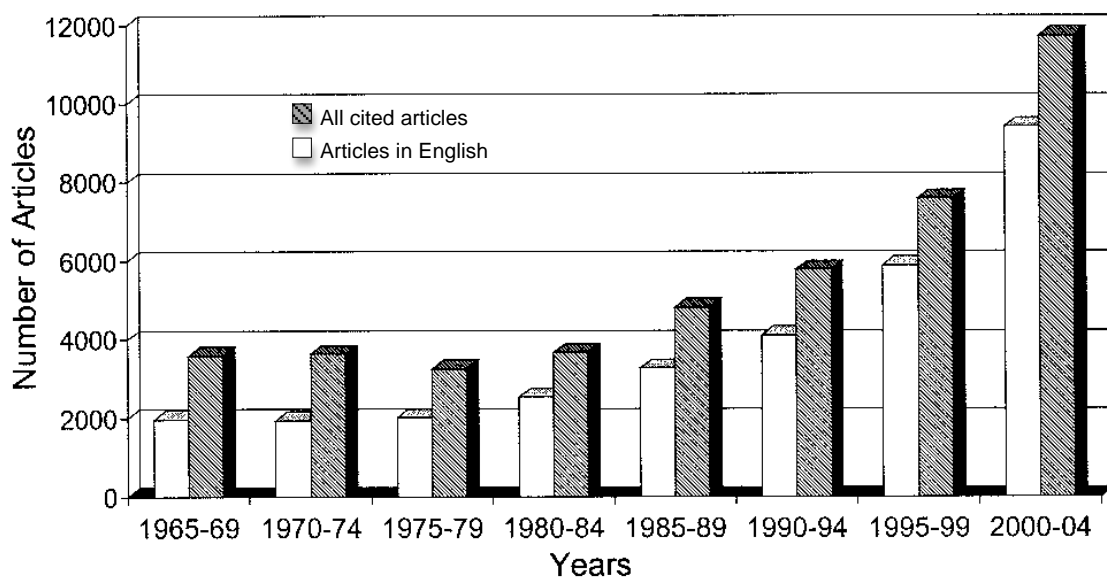
Among Australians aged 55 years and over, COPD is a far more common cause of deaths and hospitalisations than asthma. The Australian Centre for Asthma Monitoring reported that COPD accounts for ten times more deaths and six times more hospitalisations than asthma.⁴⁴¹ With 4,761 deaths attributed to it in 2006,⁸ COPD is a major cause of death in Australia, ranking fifth among the common causes of death in the country.² Furthermore, COPD is associated with a level of disability in about 34% of sufferers, rising to 68% in those aged 65 years and over,² and it is the third leading cause of burden of disease in Australia.⁴⁴²

Because of the high prevalence of the disease and the potential for severe disability, COPD represents a substantial economic and social burden. In 2008, the financial cost of COPD was \$8.8 billion.⁷ Of this, \$6.8 billion (76.6%) was productivity lost due to lower employment, absenteeism and premature deaths of Australians with COPD.

In the past, imprecise and variable definitions of COPD, as well as under-recognition and under-diagnosis, have made it difficult to quantify the prevalence, morbidity and mortality of the condition. Despite the escalating problem, COPD has been an orphan disease over the past two decades, worldwide and in Australia.⁴⁴³ This has been attributed to a lack of knowledge about the disease, a negative attitude towards the

disease (because of its mainly self-inflicted nature), a perceived lack of effective drug treatments and limited success with prevention. Fortunately, research into COPD and its management has increased substantially since the 1990s (Figure 30), and with this has come an increased awareness of the condition. The global burden of COPD has finally been recognised, with the development of evidence-based management guidelines over the last decade.^{360,443} However, the challenge remains to improve the recognition and management of COPD.

Figure 30. Number of articles listed in PubMed under the search terms ‘COPD’ OR ‘emphysema’ OR ‘chronic bronchitis’ between 1965 and 2005⁴⁴⁴



4.4 Guidelines for the management of COPD

In 1998, in an effort to bring more attention to COPD, its management and its prevention, the US National Heart, Lung and Blood Institute and the World Health Organisation formed the Global Initiative for Chronic Obstructive Lung Disease (GOLD).³⁶⁰ The GOLD Expert Panel consisted of health professionals from around the world with expertise in respiratory medicine, epidemiology, socioeconomics, public health and health education.⁴⁴⁵ The model for this initiative was the Global Initiative for Asthma, an international strategy for developing comprehensive evidence-based guidelines on asthma control and management using a committee of experts.¹⁶ The central objectives of GOLD are to:

- Increase awareness of COPD amongst governments, public health officials, healthcare workers and the general public;

- Improve prevention and management of the disease;
- Decrease COPD morbidity and mortality; and
- Encourage new research into the disease.³⁶⁰

In 2001, GOLD published a consensus report outlaying recommendations for the diagnosis, management and prevention of COPD. Importantly, the report includes grades for the weight of scientific evidence supporting each recommendation. The GOLD strategy presents a COPD management plan divided into four components:

- Assessment and monitoring of disease;
- Reduction of risk factors;
- Management of stable COPD; and
- Management of exacerbations.

Information and recommendations presented in the GOLD report are based on “the best-validated current concepts of COPD pathogenesis and the available evidence on the most appropriate management and prevention strategies.”³⁶⁰ The report is updated annually to reflect changing evidence in best practice.

In recognition of the significant burden that COPD places on the Australian community, the Australian Lung Foundation and Thoracic Society of Australia and New Zealand developed clinical practice guidelines to improve the diagnosis and management of COPD, called COPD-X (Table 53).⁴⁴⁶ The guidelines, based upon the GOLD strategy for COPD diagnosis, management and prevention, aim to affect changes in clinical practice based on sound evidence and shift the emphasis from a predominant reliance on pharmacological treatment of COPD to a range of interventions which include patient education, self-management of exacerbations and pulmonary rehabilitation.⁴⁴⁶

Table 53. Summary of the COPD-X guidelines⁴⁴³

C: Confirm diagnosis and assess severity	Evidence*
Smoking is the most important risk factor for COPD	Level I
Consider COPD in patients with other smoking-related diseases	Level I
Consider COPD in all smokers and ex-smokers older than 35 years	Level II
The diagnosis of COPD rests on the demonstration of airflow limitation which is not fully reversible	Level II
O: Optimise function	Evidence*
Inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity	Level I
Long-acting bronchodilators provide sustained relief of symptoms in moderate-to-severe COPD	Level I
Long-term use of oral corticosteroids is not recommended	Level I
Inhaled corticosteroids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations	Level II
Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation	Level I
P: Prevent deterioration	Evidence*
Smoking cessation reduces the rate of decline of lung function	Level I
General practitioners and pharmacists can help smokers quit	Level I
Treatment of nicotine dependence is effective and should be offered to smokers	Level I
Pharmacotherapies double the success of quit attempts; behavioural techniques further increase the quit rate by up to 50%	Level I
Influenza vaccination reduces the risk of exacerbations, hospitalisation and death	Level I
Inhaled corticosteroids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations	Level II
Mucolytics may reduce the frequency and duration of exacerbations	Level I
D: Develop a support network and self-management plan	Evidence*
Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes towards self-management and exercise	Level I
COPD imposes handicaps which affect both patients and carers	Level II
Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises	Level II
X: Manage eXacerbations	Evidence*
Inhaled bronchodilators are effective treatments for acute exacerbations	Level I
Oral corticosteroids reduce the severity of and shorten recovery from acute exacerbations	Level I
Exacerbations with clinical signs of infection (increased volume and change in colour of sputum and/or fever, leukocytosis) benefit from antibiotic therapy	Level II
Multidisciplinary care may assist home management	Level II

*Level I evidence = systematic review of RCTs, level II evidence = one or more RCTs.

Despite widely distributed evidence-based management guidelines, knowledge of and adherence to the guidelines amongst doctors remains suboptimal.^{4,447-451} Multiple studies demonstrate that doctors are often slow to adopt best clinical practices into their daily patterns of care,⁷⁸ and patients do not have the resources to recognise the gaps between available care and the care they receive.⁴⁵² Existing COPD guidelines have depended largely on diffusion and dissemination of their recommendations.⁴⁵³ However, only the GOLD guidelines designed an implementation strategy concurrently with the guidelines.⁴⁵⁴

Disseminating guidelines requires an appreciation of the issues that prevent translation of guideline definitions of best practice into improved patient care.⁴⁵⁴ Few data exist regarding attitudes towards existing COPD guidelines amongst doctors. In the Netherlands, Jans *et al.* began a guideline implementation project that first assessed barriers to acceptance of COPD and asthma guideline recommendations among GPs.^{455,456} They then designed an implementation strategy to overcome these barriers and promote guideline adherence in a randomised, controlled trial. One year after the project started, they found greater adherence to guideline recommendations and improved patient outcomes, as measured by lung function and symptom scores.

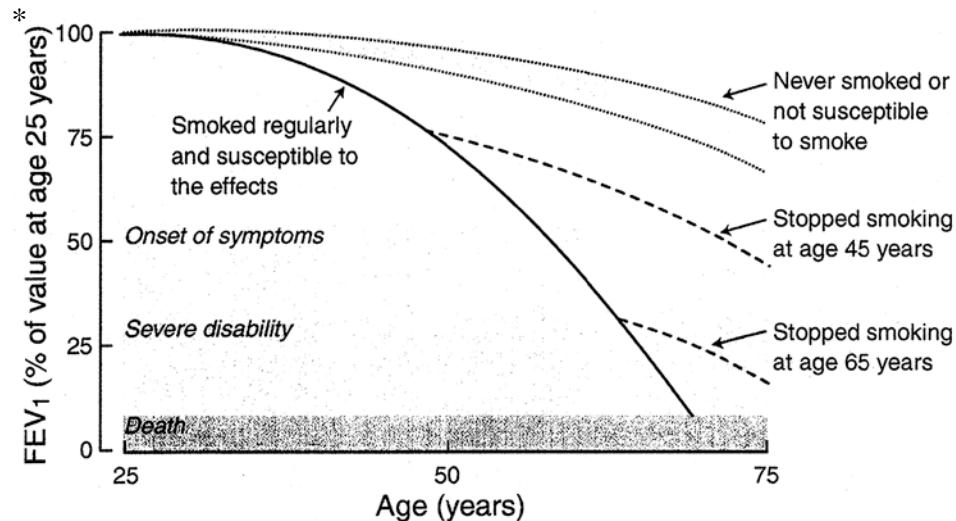
Although some COPD is managed satisfactorily in the community, there is still room for substantial improvement.⁴ Clearly, there needs to be further research into effective ways of educating patients, doctors and the general community about COPD.

4.5 Slowing lung function decline in COPD: smoking cessation

Smoking cessation is the single most effective, and cost-effective, intervention in most people to reduce the risk of developing COPD and stop its progression.³⁶⁰ While there is evidence from epidemiological studies that non-smokers can develop chronic airflow obstruction,^{457,458} tobacco smoke remains the most important cause of COPD worldwide, with up to 50% of smokers being noted to develop the condition.³⁹⁰ FEV₁ declines at about 60 mL per year in susceptible smokers, compared to the decline with normal aging of about 30 mL per year in non-smokers.⁴⁵⁹ The accelerated decline in lung function is related to current and past exposure to cigarette smoke. For example, evidence has shown that current smokers have a steeper decline in lung function than ex-smokers, while ex-smokers have a steeper decline than people who have never smoked.⁴⁶⁰ If a susceptible smoker stops smoking, he/she will not recover lost lung

function, but the subsequent rate of decline in lung function is likely to revert to normal (Figure 31).⁴⁶¹

Figure 31. Time-course of COPD⁴⁶¹



*The figure shows the rate of loss of FEV₁ for a hypothetical, susceptible smoker, and the potential effect of stopping smoking early or late in the course of COPD. Other susceptible smokers will have different rates of loss, thus reaching 'disability' at different ages. The normal FEV₁ ranges from below 80% to above 120%, so this will affect the starting point for the patient's data.

Smoking cessation is the only evidence-based treatment that has been proven to slow down the development of COPD by preventing further deterioration of lung function. The most rigorous evaluation of smoking cessation and the rate of decline in lung function was the US Lung Health Study. In a prospective RCT, 5,887 smokers with mild-to-moderate airway obstruction were randomised to one of two smoking cessation groups (smoking cessation \pm ipratropium therapy) or to a control group. Participants in the two smoking intervention groups showed significantly smaller declines in FEV₁ than those in the control group.⁴⁶² Participants who stopped smoking experienced an improvement in FEV₁ in the year after quitting (an average of 47 mL or 2%). The subsequent rate of decline in FEV₁ among sustained quitters was half the rate among continuing smokers, 31 mL versus 62 mL, comparable to that of never-smokers.⁴⁶³ Interestingly, further follow-ups showed that participants who made several attempts to quit smoking, even with subsequent relapses, had less loss of lung function at comparable cumulative doses of cigarettes than those who continued to smoke.⁴⁶⁴ However, reductions of up to 50% in smoking amount had no observable effect on the decline in FEV₁.⁴⁶⁵

There is also evidence that the slowed decline in FEV₁ is sustained years after quitting. An 11-year follow-up of the Lung Health Study demonstrated that differences in lung function between treatment groups persisted; sustained quitters had an FEV₁ rate of decline of 26.7 mL per year, intermittent quitters lost 47.5 mL per year, and those who continued to smoke throughout the 11 years declined by 60.0 mL per year.⁴⁶⁶

A 14.5-year follow-up on mortality among participants from the Lung Health Study showed that death rates were significantly higher in the usual care group than in the intervention groups (10.38 per 1000 person-years versus 8.83 per 1,000 person-years; $P < 0.05$). When survival was analysed according to smoking habit, mortality was 6.04 per 1,000 person-years in sustained quitters, 7.77 per 1,000 person-years in intermittent quitters and 11.09 per 1,000 person-years in continuing smokers. Death rates were significantly related to smoking habit from coronary heart disease ($P < 0.05$), cardiovascular disease ($P < 0.001$), lung cancer ($P < 0.01$) and other causes ($P < 0.05$).⁴⁶⁷

In addition to preventing accelerated decline in lung function, smoking cessation has been shown to significantly improve respiratory symptoms⁴⁶⁸ and airway hyper-responsiveness⁴⁶⁹ in patients with COPD. The role of smoking cessation on underlying inflammatory processes in the lungs is less clear. Data from well-designed studies regarding the effects on inflammation and remodelling are lacking, and the few available studies show contradictory results.⁴⁷⁰ It has been shown that bronchial epithelial remodelling was reduced by smoking cessation;⁴⁷¹ however, acute inflammatory processes are ongoing,⁴⁷¹⁻⁴⁷³ which may simply reflect a repair process but not ongoing damage to the lung tissue.⁴⁷⁰

The GOLD guidelines recommend that all smokers, including those who may be at risk for COPD as well as those who already have the disease, should be offered the most intensive smoking cessation intervention feasible.³⁶⁰ Currently, accepted best practice is summarised by a five-step plan for intervention, published by the US Public Health Service (Table 54).⁴⁷⁴ The plan provides a strategic framework helpful to healthcare professionals interested in helping their patients to stop smoking. Cessation of smoking is a process rather than a single event, and smokers move between various stages of being not ready, unsure, ready, quitting and relapsing before achieving long-term success. The aim of initial intervention is to advance one stage in the cessation cycle.⁴⁴³

For a patient ready to quit, appropriate treatment should be initiated, with the formulation of a quit plan. For a patient not ready to make a quit attempt, a brief intervention designed to promote the motivation to quit should be provided.⁴⁷⁵

Table 54. Brief strategies to help a willing patient to quit smoking⁴⁷⁴

1.ASK - systematically identify smokers at every visit
Implement an office-wide system that ensures that, for every patient at every visit, smoking status is queried and documented.
2.ADVISE - strongly urge all smokers to quit
In a clear, strong and personalised manner, urge every smoker to quit.
3.ASSESS - determine willingness to make a quit attempt
Ask every smoker if he or she is willing to make a quit attempt at this time (e.g. within the next 30 days).
4.ASSIST - aid the patient in quitting
Help the patient with a quit plan; provide practical counselling; provide intra-treatment social support; recommend the use of approved pharmacotherapy unless contraindicated; provide supplementary materials.
5.ARRANGE - schedule follow-up contact
Schedule follow-up contact; whether in person or via telephone.

There is good evidence that health professionals can substantially increase quitting and readiness to quit in the population. Even a brief (three-minute) period of counselling to urge a smoker to quit results in smoking cessation rates of 5-10%.⁴⁷⁶ Furthermore, collaborative efforts among health professionals are more effective than interventions by only one type of health professional; a survey of 1,723 smokers found that being asked about smoking by two or more types of professionals substantially increased the odds of recent quitting (OR 2.37; 95% CI 1.15-4.88).⁴⁷⁷


Pharmacotherapy is an important cornerstone in the treatment of nicotine dependence. Various forms of nicotine replacement therapy (NRT) (chewing gum, transdermal patches, inhalers, sublingual tablets and lozenges) are effective and well tolerated. Various forms of NRT increase the rate of quitting by 50-70%.⁴⁷⁸ Antidepressants, such as bupropion and nortriptyline, and nicotine receptor partial agonists, such as varenicline, are also very effective, but are not as well tolerated than NRT.^{479,480} It is imperative that smoking cessation interventions involve combinations of psychological and social support mechanisms, in addition to pharmacotherapy. A systematic review of RCTs on smoking cessation interventions conducted on patients with COPD, concluded

that combination treatment (psychosocial plus pharmacological intervention) is superior to no treatment or psychosocial intervention alone.⁴⁸¹

4.6 Self-management plans for COPD

Self-management interventions improve various outcomes for many chronic conditions.⁴⁸² Providing an individualised written self-management plan is a high-profile part of the fourth step of the COPD-X Plan: “develop a support network and self-management plan.”⁴⁴³ Research in self-management plans for COPD is relatively new, and variable results have been reported in the literature. The concept of self-management plans for patients with COPD is derived from their success in asthma management indicating doses and medications to take for maintenance therapy and for exacerbations. Instructions for crises are often included (Figure 32).

Figure 32. COPD self-management plan template⁴⁸³



COPD Action Plan

Patient Name:	Date of Birth:
GP Name:	GP Phone:
	After Hours Phone:
Consultant Name:	Consultant Phone:
Outreach/Community Nurse Phone:	Ambulance Phone:

USUAL TREATMENT WHEN STABLE:	Best FEV ₁ _____	Best FVC _____
	Room air O ₂ saturation _____ %	<input type="checkbox"/> CO ₂ Retainer
	Oxygen: l/min _____	hrs/day _____

MY REGULAR MEDICATION/S	STRENGTH	DOSE	ROUTE <small>MDI + SPACER / DPI / NEBULISER / ORAL</small>	HOW OFTEN
Ask your doctor about pulmonary rehabilitation or call The Australian Lung Foundation on 1800 654 301 to find out about a program near you.				
1				
2				
3				
4				
5				

MODERATE ATTACK (UNWELL BUT NOT SEVERE) • NOTIFY GP OR OTHER HEALTH PROFESSIONAL	<ul style="list-style-type: none"> • More wheezy / breathless • Increased cough and sputum • Change in colour of sputum • Loss of appetite / sleep • Taking more reliever medication than usual 	OTHER HELPFUL TIPS <ul style="list-style-type: none"> • Eat small amounts more often • Use controlled breathing techniques • Use a huff and puff cough to clear secretions • Use anxiety/stress management techniques
--	--	--


EXTRA RELIEVER	STRENGTH	DOSE	ROUTE	HOW OFTEN
1				
2				
3				

PREDNISOLONE (reducing schedule)	STRENGTH	TABS / DOSE	DAYS
start			
then			
then			
then			


ANTIBIOTIC	STRENGTH	DOSE	ROUTE	HOW OFTEN
1				
2				

SEVERE ATTACK <ul style="list-style-type: none"> • Call ambulance: 000 or ph: _____ • Show them this plan and say you have severe COPD 	My Symptoms: <ul style="list-style-type: none"> • Unable to perform normal activities e.g. dress, bathe • Fever / chills • Increased swelling of ankles • Extremely short of breath
--	--

NAME:	SIGNATURE:	DATE:
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This initiative is part of "Sail On", a National Public Health campaign to help people with COPD "put the wind back into their sails".
 The Australian Lung Foundation is grateful for financial assistance provided by:
 Sponsors – Boehringer Ingelheim, GlaxoSmithKline, Pfizer
 Supporters – Air Liquide Healthcare



live with **copd**
 An initiative of
 The Australian Lung Foundation

Much of the evidence on self-management programs for COPD comes from a Canadian multifaceted self-management program, 'Living Well with COPD,' which was one of the first studies to produce conclusive results.⁴⁸⁴ The multicentre RCT involved 191

patients from seven hospitals, and provided evidence that a multi-component, skill-oriented disease-specific self-management program can improve both short- and long-term health outcomes of COPD. The trial evaluated an intervention consisting of a comprehensive patient education program administered through weekly visits by trained health professionals over a two-month period with monthly telephone follow-up. After 12 months, hospital admissions for exacerbations of COPD were reduced by 39.8% in the intervention group compared to the usual care group ($P < 0.05$), and admissions for other health problems were reduced by 57.1% ($P < 0.05$). ED visits were reduced by 41.0% ($P < 0.05$) and unscheduled physician visits by 58.9% ($P < 0.01$). A two-year follow-up of the intervention demonstrated a reduction in all-cause hospitalisations of 26.9% and in ED visits of 21.1% in the intervention group as compared to the usual care group.⁴⁸⁵ In addition, the program demonstrated obvious economic benefits due to decreased healthcare utilisation costs.⁴⁸⁶ The 'Living Well with COPD' program has been approved by the ministry of Québec and has since been implemented in all the regions of the province.⁴⁸⁷ Most of the health professionals in Québec use this evidence-based program to educate their COPD patients.

However, a similar RCT of a self-management intervention involving a skill-oriented patient education program and near-home fitness program failed to show any positive effects.⁴⁸⁸ No differences in quality of life, symptoms or walking distance were reported between the intervention ($n = 127$) or control ($n = 121$) patients. A systematic review on self-management education for patients with COPD could not draw any conclusions about its effectiveness because of the large variation of outcome measures used in a limited number of included studies, and noted that there is an evident need for more large RCTs with a long-term follow-up, before more conclusions can be drawn.⁴⁸⁹

A systematic review showed that action plans used in COPD have positive effects on self-management knowledge, and help patients recognise and react appropriately to an exacerbation by promptly self-initiating antibiotics and oral corticosteroids.⁴⁹⁰ However, there was no evidence that these changes to patient behaviour significantly reduce morbidity, healthcare utilisation or mortality.

For example, a RCT of structured one-hour education sessions on the use of a written self-management plan and patient-initiated short courses of antibiotics and oral corticosteroids failed to show any added health benefit, in terms of health utilisation, or

self-reported outcomes, compared to usual care.⁴⁹¹ A retrospective cohort study assessing the effect of prescription of antibiotics and oral corticosteroids at the time of issuing a self-management plan also reported disappointing findings. Whilst all patients received a self-management plan and education, approximately half also received a prescription for self-administered antibiotics and oral corticosteroids. The increased use of antibiotics and/or oral corticosteroids in this subgroup were not mirrored by a reduction in unplanned medical attendances and clearly raised concerns that patient initiation without consultation may not be appropriate.⁴⁹² Similarly, a recent systematic review of five RCTs (574 patients) found evidence that action plans with limited COPD education aid recognition of, and response to, an exacerbation with initiation of antibiotics and corticosteroids. However, there was no evidence of reduced utilisation of healthcare resources or improved health-related quality of life.⁴⁹³

There is some evidence, however, that early treatment of COPD exacerbations may improve outcomes. An uncontrolled study of 128 patients with COPD who recorded respiratory symptoms daily and were encouraged to report exacerbations to the study team or their GP, found that earlier treatment was associated with a faster recovery (regression coefficient 0.42 days/days delay; $P < 0.001$).⁴⁹⁴ However, the prescription (oral corticosteroids and/or antibiotics) of treatment for all exacerbations was at the discretion of the attending physician, rather than through guided self-management.

The COPD-X Plan states that perhaps the reason for the disappointing findings regarding self-management of COPD is that “pharmacological treatment of COPD is generally less effective [as compared to pharmacological treatment of asthma] as the condition is, by definition, non-reversible.”⁴⁴³ The findings of these trials suggest that more intensive education and support may be required to significantly impact COPD outcomes.

4.7 Pulmonary rehabilitation

The non-pharmacological therapy of COPD, such as smoking cessation, education on adherence to medical therapy and collaborative self-management strategies can be given together in the form of a comprehensive outpatient pulmonary rehabilitation program. Pulmonary rehabilitation is defined as:

“...An evidence-based, multidisciplinary and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. Integrated into the individualised treatment of the patient, pulmonary rehabilitation is designed to reduce symptoms, optimise functional status, increase participation and reduce healthcare costs through stabilising or reversing systemic manifestations of the disease.”⁴⁹⁵

Pulmonary rehabilitation programs involve patient assessment, exercise training education, nutritional intervention and psychosocial support.⁴⁹⁶ The components of pulmonary rehabilitation are shown in Table 55.

Table 55. Components of comprehensive pulmonary rehabilitation programs⁴⁹⁶

1. Education, including self-management strategies
2. Upper and lower extremity exercise training, resistance training
3. Psychosocial support, when indicated
4. Encouragement of activity and exercise in the home setting
5. Outcome assessment
6. Promotion of long-term adherence

Although pulmonary rehabilitation has not been shown to have a substantial effect on the specific respiratory impairment in COPD,⁴⁹⁷ a large body of scientific evidence demonstrates its beneficial effects over multiple outcome areas. A RCT in the United Kingdom assessed the effect of outpatient pulmonary rehabilitation on the use of healthcare services and patients’ wellbeing over one year.⁴⁹⁸ There was no difference between the rehabilitation (n = 99) and control (n = 101) groups in the number of patients admitted to hospital (40 versus 41) but the number of days patients spent in hospital differed significantly (10.4 ± 9.7 versus 21.0 ± 20.7 , $P < 0.05$). Compared with the control, the rehabilitation group also showed greater improvements in walking ability and in general and disease-specific health status.

A systematic review of 31 RCTs examining the effects of pulmonary rehabilitation for COPD on health-related QOL and exercise capacity reported that in four important domains of QOL (Chronic Respiratory Questionnaire⁴⁹⁹ scores for dyspnoea, fatigue,

emotional function and mastery), the effect was larger than the minimal clinically important difference of 0.5 units (e.g. dyspnoea score: weighted mean difference = 1.0 units, 95% CI 0.8-1.3 units, n = 12 trials).⁵⁰⁰ For functional and maximal exercise capacity, the effect was small and slightly below the threshold of clinical significance for the six-minute walking distance (weighted mean difference = 48 metres, 95% CI 32-65, n = 16 trials). The authors concluded that the improvements for all outcomes were moderately large and clinically significant, and that the results strongly support pulmonary rehabilitation as part of the spectrum of the management of patients with COPD. The Australian Lung Foundation maintains a comprehensive national database of programs and can supply contact details for programs Australia-wide. Patients can enter a program either by asking for a referral from their GP and/or respiratory specialist. Many programs will also accept patients who contact them directly.

4.8 Pharmacological therapy

4.8.1 Inhaled bronchodilators

The COPD-X Guidelines state “inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity.”⁴⁴³ Inhaled bronchodilators include short- and long-acting beta-2 agonists, and short- and long-acting anticholinergics.

A systematic review of four RCTs comparing the short-acting anticholinergic ipratropium with SABAs for acute exacerbations of COPD found no evidence that the degree of bronchodilation achieved with ipratropium was greater than that using a SABA.⁵⁰¹ However, a systematic review of eleven RCTs (3,912 patients) comparing regular long-term use of ipratropium alone, or in combination with SABAs in stable COPD found small benefits for regimens containing ipratropium.⁵⁰² There was a small difference in favour of ipratropium (of borderline statistical significance) between treatments in the baseline/pre-bronchodilator FEV₁ measured at the end of the studies (mean difference 30 mL, 95% CI 0-60). Ipratropium was associated with a small but significant improvement in the baseline FVC measured at the end of the studies compared with SABAs (mean difference 70 mL, 95% CI 10-140). Combination therapy with ipratropium plus a SABA conferred benefits over a SABA alone in terms of post-bronchodilator lung function. There was no significant benefit of combination therapy in subjective improvements in QOL, but there was a reduction in the requirement for

oral steroids. The authors noted that where there were benefits in favour of ipratropium, they were small and would not support a general recommendation for the use of ipratropium over a SABA in COPD, and patients should use the short-acting bronchodilator that gives them the most improvement in their symptoms.

LABAs and long-acting anticholinergics cause prolonged bronchodilation, for 12 and 24 hours respectively, and are thus often preferred to shorter acting agents. A systematic review of seven RCTs (2,652 patients) comparing the efficacy of LABAs with ipratropium found a greater increase in FEV₁ (mean difference 60 mL, 95% CI 0-110) and morning PEF (mean difference 10.96 L per minute, 95% CI 5.83-16.09).⁵⁰³ There were no significant differences between ipratropium and salmeterol for QOL, functional capacity, symptoms, acute exacerbations or adverse effects.

A systematic review of nine RCTs (6,584 patients) comparing the long-acting anticholinergic tiotropium to other bronchodilators used for stable COPD found that tiotropium reduced the odds of a COPD exacerbation (OR 0.74, 95% CI 0.66-0.83) and related hospitalisations (OR 0.64, 95% CI 0.51-0.82) compared to placebo or ipratropium.⁵⁰⁴ Reductions in these endpoints compared to LABAs were not statistically different. However, increases in lung function tests from baseline were significantly larger with tiotropium than with placebo, ipratropium and LABAs over 6-12 months.

A retrospective analysis of one-year placebo-controlled trials indicated that tiotropium had the potential to slow the rate of decline in FEV₁.⁵⁰⁵ In 921 patients, the mean decline in FEV₁ in the first six months was 58 mL per year in the placebo group and 12 mL per year in the tiotropium group ($P < 0.01$), and in the second six months was 59 mL per year in the placebo group and 19 mL per year in the tiotropium group ($P < 0.05$). These findings led to the design of a trial to prospectively extend these observations to four years.⁵⁰⁶ The long-term benefits of tiotropium compared to placebo were recently demonstrated in the UPLIFT trial.⁵⁰⁷ A total of 5,993 patients were randomly assigned to receive tiotropium or placebo, plus any other respiratory medication, with the exception of inhaled anticholinergics, as indicated. Mean absolute improvements in FEV₁ in the tiotropium group were maintained throughout the trial, as compared with the placebo group ($P < 0.001$). However, after day 30, the differences between the two groups in the rate of decline in FEV₁ were not significant.⁵⁰⁷

The advantage of tiotropium is that it maintains bronchodilation for at least 24 hours, allowing once-daily administration. In Australia, tiotropium is currently the only long-acting bronchodilator monotherapy subsidised on the Pharmaceutical Benefits Scheme for COPD.⁵⁰⁸

Over the past decade, the cardiovascular adverse effects associated with inhaled anticholinergic medications have been debated. A media release from the US Food and Drug Administration (FDA) and the manufacturer of tiotropium (Boehringer Ingelheim) to healthcare practitioners in 2008 raised alarms about a possible increased risk of stroke in patients using tiotropium. Pooled analysis from 29 RCTs estimated that the risk of stroke was 8 per 1,000 patients treated for one year with tiotropium, and 6 per 1,000 patients treated for one year with placebo.⁵⁰⁹ The FDA warned that these preliminary results should be interpreted with caution, as while the analysis provided early information about potential safety issues, it had inherent limitations and further investigation using other data sources was required.

Following this warning, three publications highlighted concerns related to the use of inhaled anticholinergic medications and cardiovascular safety.⁵¹⁰⁻⁵¹² The most important of these was a systematic review and meta-analysis by Singh *et al.* which seemed to indicate a significantly increased risk in the primary outcome (the combined incidence of cardiovascular death, myocardial infarction or stroke amongst people with COPD using inhaled anticholinergic medications; 1.8% versus 1.2% [$P < 0.001$] for people using inhaled anticholinergic medication and control medication, respectively).⁵¹² The data for this meta-analysis came from over 13,000 participants enrolled in 17 trials. Among the individual components of this outcome, only the increased risk of stroke failed to reach statistical significance. All-cause mortality remained unaffected. This study included selected RCTs of any inhaled anticholinergic medication for the treatment of COPD where participants received at least 30 days of treatment and were assessed for cardiovascular events. This meta-analysis was criticised on a number of grounds.⁵¹³⁻⁵¹⁶ None of the included trials were designed to specifically target cardiovascular risks, and these events were not defined or assessed consistently across the included trials. The majority of trials were small and of short duration, which resulted in few events occurring. The meta-analysis was also criticised for combining the results of placebo-controlled and active-controlled trials and not taking into account varying treatment discontinuation rates within trials. Interestingly, when data from only

trials involving tiotropium were considered, there was no statistically significant difference in adverse cardiovascular outcomes compared to control, while there was a statistically significant increase in the incidence of adverse cardiovascular outcomes when ipratropium was compared to control.

Fortunately, additional data is now available to address this area of uncertainty. Firstly, the UPLIFT study, which compared long-term tiotropium to placebo in almost 6,000 patients with COPD who were not already taking inhaled anticholinergic medications.⁵⁰⁷ Patients were at least 40 years of age and had a FEV₁ of 70% or less after bronchodilation. The occurrences of serious adverse events (including cardiovascular events) were included as secondary endpoints of the study. There was no increase in the risk of adverse cardiovascular events in this study; in fact, the rate of serious adverse cardiac events was statistically significantly lower in patients receiving tiotropium. Secondly, the cardiovascular safety of tiotropium was recently evaluated in an analysis of data from 30 RCTs of greater than four weeks duration comparing tiotropium to placebo.⁵¹⁷ Patients from these trials were included if they had spirometry-confirmed COPD, ≥ 10 pack-year smoking history and age ≥ 40 years. Importantly, standardised assessment of adverse events was conducted (this was an important criticism of the previous meta-analysis). More than 19,000 patients from these trials were included. In this meta-analysis, tiotropium was associated with a reduction in the risk of all-cause mortality, cardiovascular mortality and cardiovascular events. In light of these recent results, the FDA issued a follow-up to their previous early communication regarding tiotropium, making the following statement:

“The available data do not support an association between the use of Spiriva® (tiotropium) and an increased risk for these serious adverse events (stroke, myocardial infarction or death from a cardiovascular cause).”⁵¹⁸

Recent data concerning the cardiovascular outcomes associated with the use of short-acting inhaled anticholinergics is not so positive. Given the investment required, it is unlikely that prospective trials to define the cardiovascular safety of inhaled ipratropium will ever be conducted. Therefore, healthcare professionals must consider the results of the Singh *et al.* meta-analysis, conducted in 2008,⁵¹² and additional data from recent cohort studies⁵¹⁹ which raise concerns that its use might be associated with a small

increase in the risk of adverse cardiovascular events. The reasons for this apparent discrepancy are unknown. Pharmacologically, it is not clear why short-acting inhaled anticholinergic medications would affect the cardiovascular system differently than longer-acting agents. Regardless of the most recent trial data, the following statement seems to be a useful clinical viewpoint from a US medical specialist:

“Patients with COPD who are taking long-term anticholinergics should be closely monitored for the development of the signs and symptoms of cardiovascular disease. However, this is best practice for almost all patients with COPD, since they are already at elevated risk for cardiovascular morbidity and mortality.”⁵²⁰

4.8.2 Inhaled corticosteroids

The progression of COPD is associated with inflammation.³⁶³ The COPD-X guidelines recommend that anti-inflammatory drugs such as ICS should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations.⁴⁴³

A systematic review of 47 RCTs (13,139 patients) found that long-term use of ICS (more than six months) did not significantly reduce the rate of decline in FEV₁ (weighted mean difference 5.80 mL/year with ICS over placebo, 95% CI 0.28-11.88), or mortality in COPD patients (OR 0.98, 95% CI 0.83-1.16). However, long-term use of ICS reduced the mean rate of exacerbations (weighted mean difference -0.26 exacerbations per patient per year, 95% CI -1.83 to -10.60), and slowed the rate of decline in QOL, as measured by the St George’s Respiratory Questionnaire (weighted mean difference -1.22 units/year 95% CI -1.83 to -0.60). The authors concluded that patients and health professionals should balance the potential benefits of ICS (reduced rate of exacerbations, reduced decline in QOL) against the adverse effects (oral thrush, hoarseness and unknown long-term adverse effects).⁵²¹

4.8.3 Combination therapy

Most studies that have explored the value of combination therapy have shown significant improvements over single agents alone.^{522,523} In a six-month RCT of 1,704 patients with moderate to very severe COPD, the combination of budesonide and

eformoterol demonstrated significant improvements in lung function, dyspnoea and QOL scores compared to either agent alone.⁵²⁴ Budesonide/eformoterol 320/9 µg demonstrated significantly greater improvements in pre-dose FEV₁ versus budesonide ($P = 0.026$) and one-hour post-dose FEV₁ versus budesonide ($P < 0.001$). The combination therapy had a safety profile comparable with that of the single components and placebo.

The TORCH (TOward a Revolution in COPD Health) study compared salmeterol 50 µg plus fluticasone 500 µg with placebo, salmeterol alone or fluticasone alone in 6,112 patients.⁵²⁵ Compared with placebo, salmeterol and fluticasone in combination reduced the risk of death at any time during the three-year study period by 17.5% ($P = 0.05$). The risk of death in the salmeterol group and the fluticasone group did not differ significantly from placebo. The salmeterol/fluticasone combination was significantly better than each of its components alone in preventing exacerbations, and this benefit was accompanied by sustained improvements in health status and FEV₁.

Although to date none of the currently available pharmacological interventions have been shown to alter the rate of decline in lung function in COPD patients, in a post hoc analysis of the TORCH study, the spirometry results in 5,343 patients over three years suggested that the combination of salmeterol/fluticasone 50/500 µg may have a beneficial effect on lung function in the medium term.⁵²⁶ Salmeterol plus fluticasone reduced the rate of FEV₁ decline by 16 mL per year compared with placebo (95% CI 7-25, $P < 0.001$). Although the difference was smaller for both fluticasone and salmeterol alone compared with placebo (13 mL per year, 95% CI 5-22, $P < 0.05$), the rates of decline were similar among the active treatment arms.

The INSPIRE (Investigating New Standards for Prophylaxis in Reducing Exacerbations) study compared the relative efficacy of salmeterol/fluticasone 50/500 µg combination twice daily and tiotropium 18 µg once daily in preventing exacerbations and related outcomes in 1,323 patients with severe and very severe COPD.⁵²⁷ Interestingly, the study showed no difference in reduction of exacerbations between the groups, although patients receiving the salmeterol/fluticasone combination had better health status as measured by the St. George's Respiratory Questionnaire (total score difference 2.1 units, 95% CI 0.1-4.0; $P < 0.05$) and had better survival (all-cause mortality rate 3% versus 6% with tiotropium, $P < 0.05$). This was the first study to

directly compare an ICS/LABA combination and a long-acting anticholinergic, and has important implications for the choice of therapy in the management of severe COPD.

There is evidence that the addition of fluticasone to tiotropium and salmeterol improves COPD outcomes. A study of 449 patients with COPD demonstrated tiotropium plus fluticasone/salmeterol improved lung function ($P < 0.05$) and disease-specific QOL ($P < 0.05$) and reduced the number of hospitalisations for COPD exacerbation (RR 0.53, 95% CI 0.33-0.86) compared with tiotropium plus placebo.⁵²⁸ In contrast, tiotropium plus salmeterol did not statistically improve lung function or hospitalisation rates compared with tiotropium plus placebo.

4.8.4 Methylxanthines

In practice, methylxanthines are rarely used because of their narrow therapeutic index and potential for significant adverse effects. Systematic reviews have provided evidence that theophylline improves FEV₁^{529,530} and arterial blood gas tensions⁵³⁰ compared to placebo in patients with COPD. All studies that have demonstrated efficacy of theophylline in COPD were done with slow release preparations. Low dose (100 mg twice daily) slow release theophylline has been shown to reduce exacerbations in patients with COPD but does not increase post-bronchodilator lung function.⁵³¹

Theophylline may be useful as adjunctive therapy in combination with a LABA in carefully selected patients. A 12-week study comparing salmeterol, theophylline, and a combination of both in 943 patients with moderate-to-severe COPD showed that the combination was more effective than either drug alone.⁵³² Patients taking the combination therapy had greater improvements in pulmonary function, greater decreases in symptoms, dyspnoea and SABA use and fewer COPD exacerbations ($P < 0.05$ versus theophylline). Salmeterol treatment was associated with fewer drug-related adverse events than either treatment that included theophylline ($P < 0.05$). A seven-year study of 36,492 patients with COPD found that patients treated with theophylline (either alone or in addition to ICS) were less likely to have moderate-to-severe COPD exacerbations than patient treated with LABA (either alone [OR 0.89, 95% CI 0.84-0.95] or in addition to ICS [OR 0.89, 95% CI 0.87-0.92]).⁵³³ However, patients treated with theophylline were more likely to have moderate-to-severe COPD exacerbations than patients treated with ICS (RR 1.07, 99% CI 1.04-1.10), and this

association was even stronger than patients who had a least three exacerbations in the year prior to cohort entry (RR 1.28, 95% CI 1.19-1.38).

There is currently no evidence supporting the use of methylxanthines for COPD exacerbations. A systematic review of four RCTs (169 patients) comparing the efficacy of methylxanthines to placebo for COPD exacerbations found no clear indication of whether there was benefit in terms of reduced symptoms or hospital admissions, but adverse effects were found to be more common with methylxanthines.⁵³⁴ The odds of nausea or vomiting were significantly higher for patients receiving a methylxanthine (OR 4.6, 95% CI 1.7-12.6) than for patients receiving placebo. Trends toward more frequent tremor (OR 1.8, 95% CI 0.7-4.6), palpitations and arrhythmias (OR 4.1, 95% CI 0.9-19.6) were also observed.

According to best practice guidelines, theophylline should be considered only for patients in whom other treatment has failed to control symptoms adequately (e.g. after a trial of short-acting bronchodilators and long-acting bronchodilators), or in patients who are unable to use inhaled therapy.⁴⁴³ With close monitoring of individual patients and their serum drug levels, it appears that beneficial effects may be obtained in those symptomatic from COPD despite first-line bronchodilator therapy.

4.8.5 Systemic corticosteroids

Short courses of systemic corticosteroids are recommended for severe exacerbations of COPD.⁴⁴³ A systematic review of ten RCTs (921 patients) found significantly fewer treatment failures (defined as a return to the ED or doctor's office, a deterioration of COPD leading to change in treatment, or death) within 30 days in patients given systemic corticosteroid treatment (OR 0.48, 95% CI 0.34-0.68).⁵³⁵ There were also significant improvements in breathlessness and blood gases 6-72 hours after treatment. There is also evidence that high doses (≥ 30 mg) of oral prednisolone improves FEV₁ over a short period (weighted mean difference 53.30 mL, 95% CI 22.21-84.39 after two weeks treatment).⁵³⁶ The most appropriate corticosteroid dosage regimen for exacerbations of COPD remains controversial, as the regimens used in RCTs differ greatly, and clinical and systematic reviews do not provide adequate guidance on these regimens.⁵³⁷ Clinical guidelines, in accordance with safety and efficacy data, recommend 30 to 50 mg of oral prednisolone daily for up to two weeks.^{369,443}

The long-term use of oral corticosteroids for COPD is not recommended.⁴⁴³ A systematic review of 24 RCTs found that long-term use did not slow the decline in lung function, and increased the risk of adverse effects such as diabetes and osteoporosis.⁵³⁶ Switching from the use of oral to inhaled corticosteroids is not associated with adverse outcomes. In one RCT involving 38 patients who were dependent on oral corticosteroids, there were no differences in disease exacerbation, quality of life or lung function when patients switched from oral to inhaled therapy.⁵³⁸

4.8.6 Antibiotics

Current evidence does not support long-term antibiotic use to prevent exacerbations in patients with COPD. A systematic review of nine RCTs (1,055 patients) found that prophylactic antibiotics in chronic bronchitis/COPD had a small but statistically significant effect in reducing the days of illness due to exacerbations.⁵³⁹ However, they do not have a place in routine treatment because of concerns about the development of antibiotic resistance and the possibility of adverse effects.

A systematic review of eleven RCTs (917 patients) found that the use of antibiotics in acute COPD exacerbations, regardless of choice, reduced the risk of short-term mortality by 77%, decreased the risk of treatment failure by 53% and the risk of sputum purulence by 44%; with a small increase in the risk of diarrhoea.⁵⁴⁰ Antibiotics are therefore recommended for exacerbations with an increase in cough, dyspnoea, sputum volume or purulence.

4.8.7 Oxygen therapy

Continuous supplemental oxygen should be used to improve exercise capacity and survival in patients with moderate-to-severe COPD who have severe hypoxaemia ($\text{PaO}_2 < 55$ mm Hg or $\text{SaO}_2 < 88\%$).⁴⁴³ A systematic review of six RCTs (567 patients) found that long-term home oxygen therapy improves survival in a selected group of patients with severe hypoxaemia ($\text{PaO}_2 < 55$ mm Hg).⁵⁴¹ Furthermore, there is evidence that short-term ambulatory oxygen improves exercise capacity.⁵⁴² However, further research is required to determine which COPD patients benefit from ambulatory oxygen, how much oxygen should be provided and the long-term effects of ambulatory oxygen.

4.8.8 Mucolytics

Mucolytics should be considered in patients with COPD who have a chronic cough productive of sputum.⁴⁴³ A systematic review of 26 RCTs (7,335 patients) reported a 20% reduction in the number of exacerbations per patient with oral mucolytics compared to placebo.⁵⁴³ However, no differences in lung function between the treatments were reported. Bearing in mind there are significant QOL and healthcare costs that result from having exacerbations, health professionals and patients will need to judge whether the reduction in exacerbation rate is large enough to warrant daily treatment with these medicines. Benefit may be greater in patients who have frequent or prolonged exacerbations, or those who are repeatedly admitted to hospital with COPD exacerbations, although data from RCTs do not permit a test of this hypothesis.⁵⁴³

4.9 Medication adherence and persistence in COPD

4.9.1 Definitions of adherence and persistence

Optimal disease management requires good adherence and persistence. The World Health Organisation states “poor adherence to long-term therapies severely compromises the effectiveness of treatment making this a critical issue in population health both from the perspective of quality of life and of health economics.”⁵⁴⁴

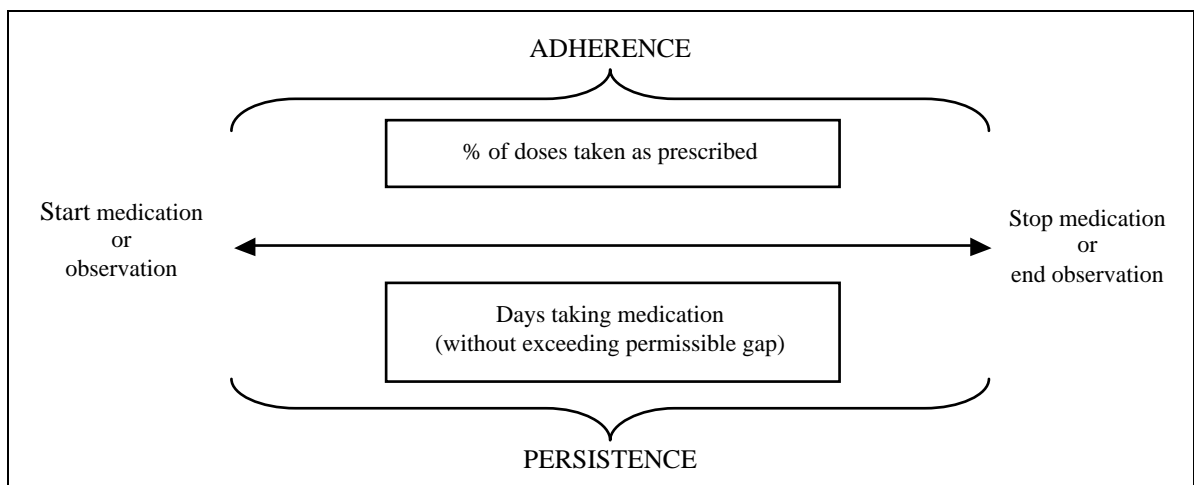
The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) defines medication adherence or compliance as “the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen.”⁵⁴⁵ Medication adherence therefore refers to the act of conforming to the recommendations made by the provider with respect to timing, dosage and frequency of medication taking. Although the terms adherence and compliance are often used interchangeably, adherence is preferred by many healthcare providers as it implies a co-operative, two-way relationship versus the one-way interaction inferred from the term compliance.⁵⁴⁶ The term adherence is intended to be a statement of fact rather than a judgemental term implying blame of the prescriber, patient or treatment.⁵⁴⁷

Non-adherence can be broadly classified as intentional or unintentional. Intentional non-adherence is an active process in which the patient chooses to deviate from the treatment regimen, whereas unintentional non-adherence is a passive process in which the patient may be careless or forgetful about properly adhering to the treatment

regimen.⁵⁴⁸ These two types of non-adherence have been associated with different patient characteristics and should therefore be recognised as two different phenomena. For example, while intentional non-adherence seems to reflect the patient's balance of reasons for and against taking medication, unintentional non-adherence is less strongly associated with decision balance, and more so with demographics.⁵⁴⁹

Medication persistence, as defined by ISPOR, refers to “the duration of time from initiation to discontinuation of therapy.”⁵⁴⁵ While medication adherence refers to medication-taking behaviour within a specific time interval, medication persistence attempts to capture the amount of time that a patient remains on chronic drug therapy.⁵⁵⁰ While no overarching term combines medication adherence and persistence,⁵⁴⁵ by definition, adherence necessitates persistence. For example, a patient must be persistent in order to display adherent behaviour. Furthermore, to be classed as persistent, a patient must display mostly adherent behaviour, as persistence analyses must include a pre-specified limit on the number of days allowed between prescription refills. This ‘permissible gap’ should be the maximum allowable period patients could go without a dose and not anticipate reduced or suboptimal outcomes.⁵⁴⁵ Figure 33 displays how medication adherence and persistence can be quantitatively defined. Adherence is usually measured over a period of time and reported as a percentage, whereas persistence is usually reported in terms of number of days for which therapy was available. Both terms may also be reported as dichotomous variables (adherent/non-adherent or persistent/non-persistent) according to pre-defined criteria at the end of a pre-specified time period.

Figure 33. Quantitative definitions of compliance and persistence⁵⁴⁵



Medication adherence and persistence can be estimated using a variety of methods (Table 56). Traditional assessment measures such as patient self-report are known to significantly over-estimate medication adherence.^{260,551} Likewise, prescription records may be inaccurate, as they do not verify drug administration.^{552,553} It is recognised that a gold standard measure to assess medication taking behaviour does not exist.⁵⁵²

Table 56. Methods of measuring adherence^{546,554}

Method	Advantages	Disadvantages
Directly observed therapy	Most accurate	Patients can hide pills in the mouth and then discard them; Impractical for routine use
Biological assay	Objective	Expensive; ⁵⁵⁵ Results may be altered by the patient improving their medication adherence in the days before the assay ⁵⁵⁶⁻⁵⁵⁸
Patient self-report	Simple; Inexpensive	Results are easily distorted by the patient, adherence often over-estimated ^{260,551}
Pill counts	Objective; Quantifiable; Easy to perform	Results easily altered by the patient (e.g. pill dumping) ⁵⁵⁹
Rates of prescription refills	Simple Easy to obtain data	Does not verify drug administration; ⁵⁶⁰ Ideally requires a centralised pharmacy system ⁵⁶¹
Assessment of the patient's clinical response	Simple	Factors other than medication adherence can affect clinical response

4.9.2 Rates of adherence and persistence in COPD

COPD is a chronic disease requiring daily use of medication for most patients for the rest of their lives. An important contributing factor to both morbidity and mortality of patients with COPD is their non-adherence and non-persistence with drug therapy.⁵⁶² However, adherence to long-term preventative COPD medication regimens has been estimated to be as low as 28%.⁵⁶³ Furthermore, patients with poor adherence to COPD medication have been shown to have significantly better adherence rates to co-morbidities treated with oral medications.⁵⁶⁴

A Canadian study that assessed patterns of persistence with inhaled medications for COPD found low rates of persistence with long-term treatment.⁵⁶⁵ It was found that 15-63% of patients continued on the prescribed drug for more than six months, which decreased to 7-53% at 12 months and 55-47% at 18 months. Patients who had no prior

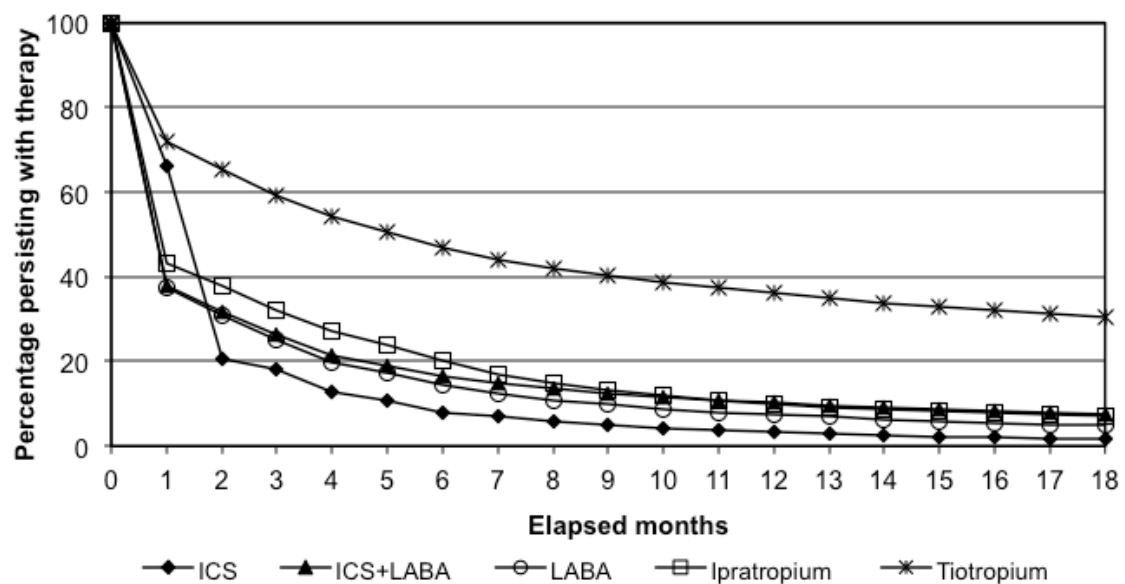
experience with inhaled medication in the previous year had significantly shorter treatment persistence for all inhaled medications ($P < 0.0001$). The authors concluded that further research is needed to pursue reasons why patients do not continue on treatment.⁵⁶⁵

A large analysis of medication record in the Netherlands, found that about 37% of new users of tiotropium continued treatment for one year, compared with 14% for ipratropium, 13% for LABAs and 17% for LABAs in combinations with ICS.⁵⁶⁶ Multivariate analyses showed that patients using tiotropium were 2-3 times more persistent with their therapy than patients using ipratropium (RR 2.0, 95% CI 1.8-2.3), LABAs (RR 2.9, 95% CI 2.4-2.6), or LABAs in combination with ICS (RR 2.4, 95% CI 2.1-2.8).

A recent Australian study also found low rates of long-term persistence with inhaled respiratory medication. The study was a retrospective assessment of de-identified prescription claims data in a 10% random sample of Australian Medicare beneficiaries, between June 2003 and March 2005.⁵⁶⁷ Patients initiated on inhaled beclomethasone, budesonide, fluticasone, eformoterol, salmeterol, budesonide plus eformoterol, fluticasone plus salmeterol, ipratropium and tiotropium were included. Medications were further divided into major drug classes, namely ICS, LABAs, combination ICS plus LABAs, and short- and long-acting anticholinergics. Patients were treated as being initiated to therapy if the medication had not been supplied in the previous 12 months. Discontinuation was defined as the absence of a claim for the initiated drug for three consecutive months or more. Patients were subdivided as 'naïve' (no inhaled medication in the previous year) or 'experienced' (previous or current treatment).

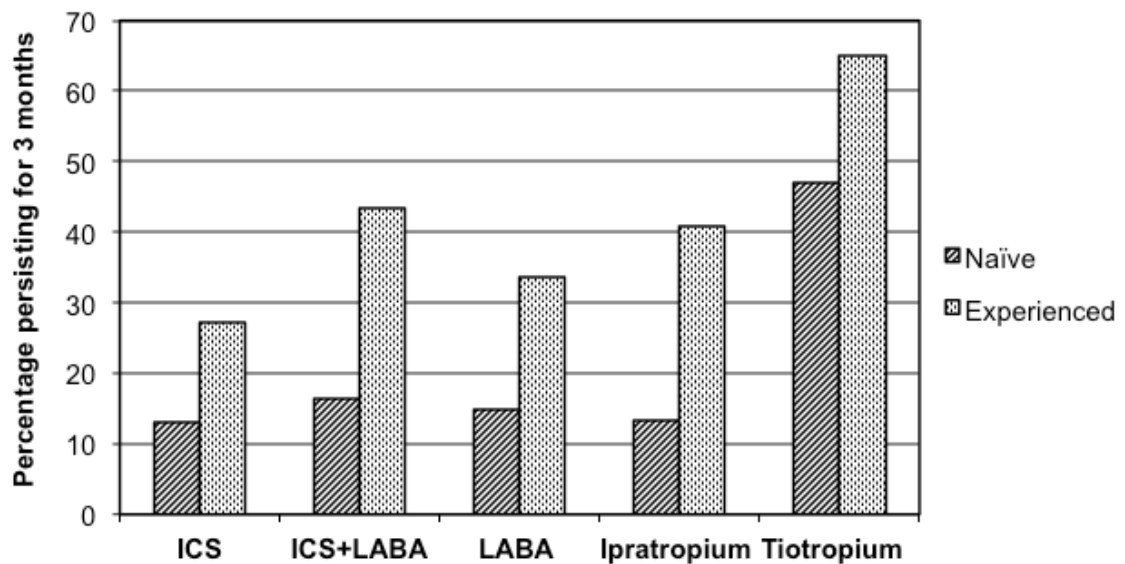
The database included 110,470 patients (66,825 naïve and 43,645 experienced) who were initiated on at least one of the study medications. Eight to 47% of patients persisted with therapy for six months, which decreased to 3-36% at 12 months and 2-30% at 18 months. Persistence with tiotropium was increased compared with other medications (Figure 34).

Figure 34. Treatment persistence over 18 months for all study drug classes



Fewer naïve patients persisted with all medications than experienced patients, which was evident after only three months of therapy (Figure 35).

Figure 35. Treatment persistence after three months for naïve and experienced patients

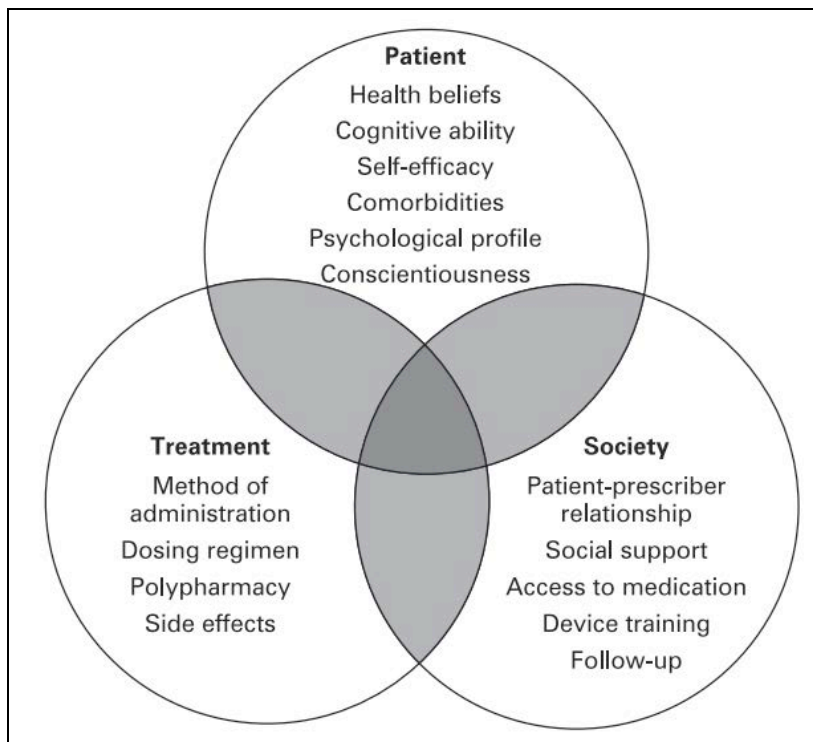


The findings of this study are consistent with reports that COPD is poorly managed in Australia,⁴ despite the availability of safe and effective respiratory medication. In keeping with international reports,^{565,566} persistence with tiotropium was higher compared with other respiratory medications, although long-term persistence was still suboptimal.

Poor adherence and persistence with medication is likely to be associated with an increased morbidity and mortality of COPD. This hypothesis was tested in a retrospective analysis of adherence of the TORCH study database.⁵⁶² The TORCH study was a RCT comparing inhaled salmeterol and fluticasone with placebo in moderate-to-severe COPD over three years. Good adherence was defined as an average adherence to study medications of more than 80% over the whole period of the study, and poor adherence was defined as an average adherence of 80% or less. Of the 4,880 patients (79.8%) with good adherence, 11.3% died in contrast to 26.4% among the 1232 patients (20.2%) with poor adherence. The annual rates of hospitalisations for exacerbations were 0.15 and 0.27, respectively. The association between adherence and mortality remained unchanged and statistically significant after adjusting for other factors related to prognosis with a hazard ratio of 0.40 (95% CI 0.35-0.46, $P < 0.001$). Similarly, the association between adherence and hospitalisation remained unchanged and significant in multivariate analysis, with a rate ratio of 0.58 (95% CI 0.44-0.73, $P < 0.001$). The authors concluded that further research is need to understand these strong associations.⁵⁶²

4.9.3 Barriers to adherence and persistence in COPD

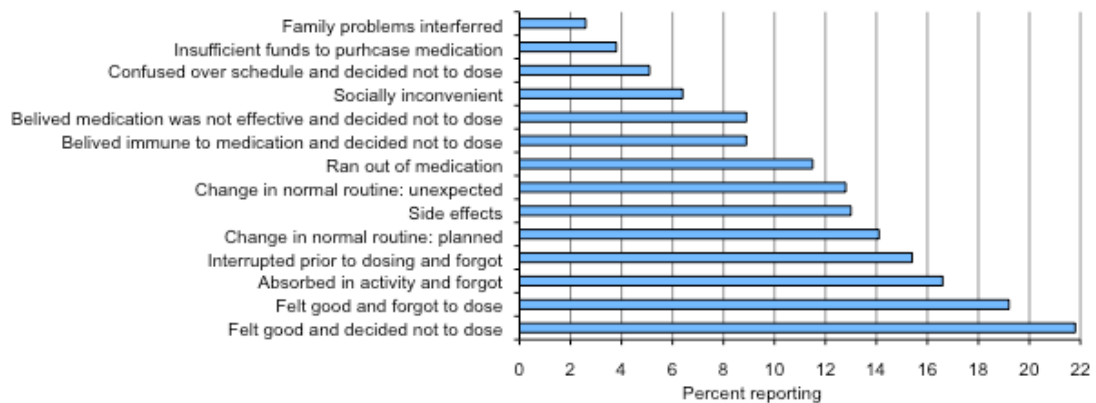
Only a limited number of studies have specifically examined patient adherence with COPD therapy and, in general, less is known about adherence in COPD than in asthma.⁵⁶⁸ Medication adherence and persistence in COPD are complex concepts, and may be influenced by multiple factors including social/environmental, patient-related and treatment-related factors (Figure 36).

Figure 36. Factors likely to influence patient adherence and persistence in COPD⁵⁶⁹

Patients with COPD have many potential risk factors for poor adherence and persistence.⁵⁷⁰ COPD being a condition characterised by multiple co-morbidities,⁵⁷¹⁻⁵⁷⁴ and patients are likely to be on complex medication regimens consisting of time-contingent and symptomatic oral and inhaled respiratory medications, as well as other medications.⁵⁷⁵

One of the earliest studies of adherence in COPD, conducted by Dolce *et al*, examined self-reported adherence in 78 outpatients being treated at a medical centre in the US.⁵⁷⁵ Patients reported that they were prescribed an average of six medications, requiring different dosage regimens and modes of administration. More than 50% of patients reported regularly under-using prescribed medications. Furthermore, 31% of patients reported deliberately deciding not to dose. This decision was most frequently associated with feeling good but was also related to concerns about side effects, beliefs that the medication would not be effective, concerns that they would become immune to the medication and confusion about actual dosing schedules (Figure 37). Patients also reported that they were more likely to overuse rescue medications when they were experiencing respiratory distress.

Figure 37. Common causes of poor adherence in COPD patients⁵⁷⁵



An Australian study aimed to identify the predictors of medication adherence in patients with COPD, using self-administered questionnaires, contrasting the health beliefs, experiences and behaviours of COPD patients self-reporting good adherence with those patients reporting suboptimal adherence to their medication.⁵⁷² Differences in knowledge about the illness and treatment, faith in and satisfaction with the treatment and doctors, and intentional and unintentional deviations from the recommended treatment were detected between the adherent and less adherent groups. The questionnaire items “I vary my recommended management based on how I am feeling” and “I get confused about my medications” were found to be significant independent predictors of non-adherence.⁵⁷² This study demonstrated that both intentional and unintentional forms of non-adherence are important in COPD patients. An earlier US study reported that nearly one-third of patients with COPD reported missing prescribed doses of medication because they deliberately decided not to dose, a decision that was most commonly associated with ‘feeling good.’⁵⁷⁵

The route of administration can influence treatment persistence. Although the pattern of early discontinuation has been demonstrated with other medication classes, oral medications usually have a larger proportion of patients persisting for a year, compared with inhaled medications.⁵⁷⁶ COPD patients using tiotropium have been shown to be more persistent with their therapy than patients using other inhaled medication.^{565,566} Once daily-dosing of tiotropium compared with LABA and ICS, which are mostly twice-daily, and ipratropium, which is mostly four times daily, may account for the enhanced persistence with tiotropium. Indeed, simplification of dosing regimens by reducing dose frequencies has been shown to increase medication adherence in several chronic diseases.⁵⁷⁷

The World Health Organisation states “interventions aimed at improving adherence would provide a significant positive return on investment through primary prevention (of risk factors) and secondary prevention of adverse health outcomes.”⁵⁴⁴ While a number of studies have reported suboptimal rates of medication persistence in COPD,^{565,566,578,579} relatively little is known about the reasons why patients with COPD do not continue on their prescribed medication. Before targeted interventions can be performed, it is essential that the factors affecting adherence and persistence be identified and understood.

CHAPTER FIVE:

UNDERSTANDING MEDICATION PERSISTENCE IN PATIENTS WITH COPD

5.1 Aim and objectives

This study aimed to understand the reasons why patients with COPD do and do not persist with prescribed medication. Specifically, the objectives were to:

- Identify the drivers and barriers of persistence with tiotropium in patients with COPD;
- Identify the significant independent predictors of persistence with tiotropium;
- Determine whether prior experience with respiratory medication determines the likelihood of persisting with tiotropium; and
- Understand patients' rational and emotional thoughts and feelings towards their condition and medication.

5.2 Methods

5.2.1 Study design and setting

This study was designed to be a descriptive analysis of medication persistence in patients with COPD. The study utilised community pharmacists and their computerised prescription data to help identify patients who had ceased to persist with tiotropium therapy. Both quantitative and qualitative measures relating to persistence were explored. Participants were identified from community pharmacy dispensing records, in Tasmania, Australia.

5.2.2 The data mining software

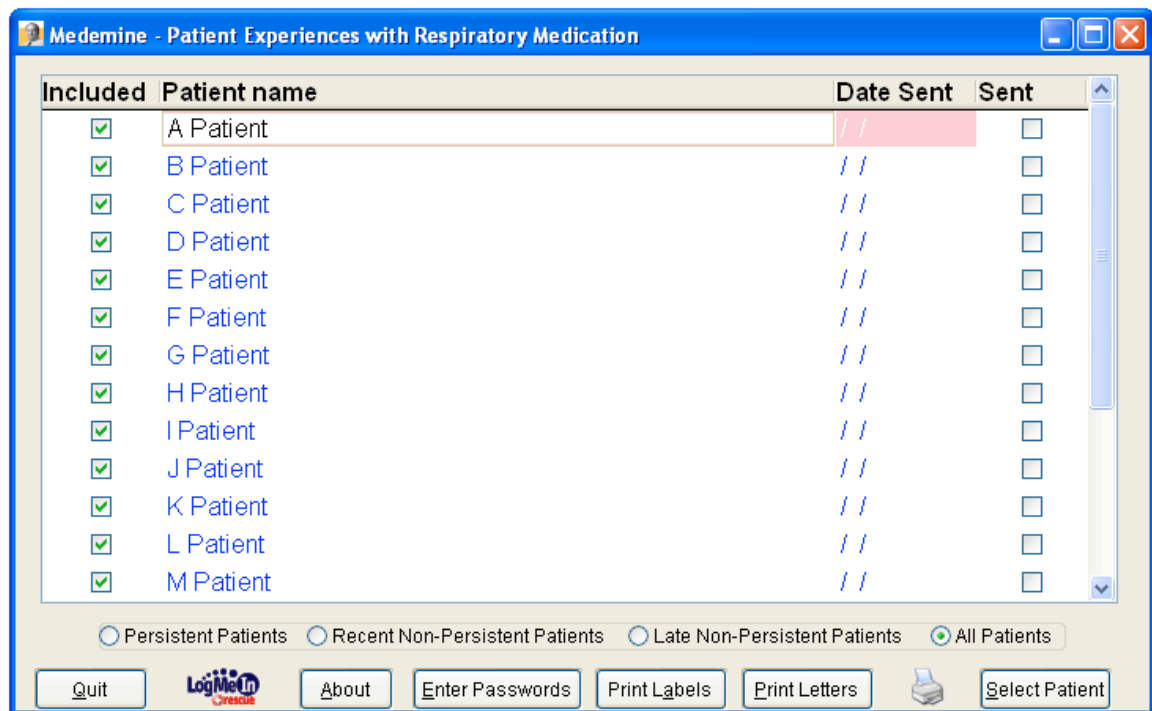
The information technology development under this study involved modifying the existing MedeMine software application, used in previously described studies, to identify patients with COPD, as evidenced by the recent use (or at least, dispensing) of tiotropium. By definition, understanding the drivers and barriers of persistence with tiotropium required researching both persistent and non-persistent patients. Therefore, a specific identification algorithm was written into the software application to enable

detection of patients who were likely to be either persistent or non-persistent with tiotropium.

Once the program was installed on a dispensing computer, the dispensing history was interrogated and a list of patients identified as having received tiotropium in the previous 12 months was generated. Patients were automatically identified as ‘persistent’ if they had received at least nine supplies of tiotropium in the preceding 12 months, including at least two units in the past 90 days. Patients were identified as ‘non-persistent’ if they had received one to four supplies of tiotropium in the preceding 12 months, with nil supplies in the subsequent 65 days. Non-persistent patients were further classified as ‘recent non-persistent’ if they had received their past supply of tiotropium in the last six months, or ‘late non-persistent’ if they had received their last supply in the past 7-12 months. This further classification was a useful tool to determine the likelihood of patients’ ability to accurately recall their reason(s) for non-persistence.

For research purposes, an additional classification dimension was used, namely whether patients had received inhaled respiratory medication (excluding SABAs) in the year preceding their first tiotropium supply. The reasoning behind this additional classification was that previous research has demonstrated that patients who had not used regular inhaled respiratory medication in the year before their first tiotropium prescription tended to have significantly shorter treatment persistence.⁵⁶⁵ Patients were classed ‘respiratory medication (RM)-naïve’ if they had not received any inhaled respiratory medication (excluding SABAs and nebulised medication) in the 12-month period prior to their first supply of tiotropium, or ‘RM-experienced’ if they had received any inhaled respiratory medication (excluding SABAs and nebulised medication) in the 12-month period prior to their first supply of tiotropium.

Figure 38 displays a screen shot of an example list of patients identified using ‘MedeMine-for-COPD.’ Functions of the software application allowed for viewing all identified patients (as shown), or persistent, recent non-persistent or late non-persistent patients separately. Personalised letters and address labels could also be printed from this screen.

Figure 38. List of identified patients in MedeMine-for-COPD

A patient's dispensing information could be viewed in detail by highlighting the patient's name and clicking on 'select patient.' Dispensing information on the MedeMine-for-COPD screen, as shown in Figure 39, was engineered to look the same as that seen in the Fred dispensing system so that pharmacists would have an instant familiarity with the layout and presentation of the information. The patient screen used four tabs ('Spiriva dispensings,' 'collated history,' 'all dispensing history' and 'feedback'). The first three tabs displayed the patient's history in different ways; the 'Spiriva dispensings' tab showed details of all Spiriva[®] (tiotropium) supplies, the 'collated history' counted the number of supplies of each medication dispensed and 'all dispensing history' displayed a sequential history for the patient. How much information was displayed was determined by selecting 'months history to display' (1, 3, 6, 9, 12 or all). The 'feedback' tab gave the pharmacist the facility to enter free text relating to the patient. Patients could be excluded from the study by selecting a reason from the drop-down 'reason not included' menu on the top right hand side of the screen.

Figure 39. Viewing patient dispensing history in MedeMine-for-COPD

The screenshot shows a window titled "Viewing Spiriva trial for A PATIENT". It contains a patient information box on the left, a "Reason not included" dropdown, a "Sent to Patient" date/time field, and a "Months History to display" selection. Below these are four tabs: "Spiriva Dispensings", "Collated History", "All Dispensing History" (which is selected), and "Feedback". The "All Dispensing History" tab displays a table with columns: Disp, Drug Name, Qty, Directions, Doc, Rpt, Dp, \$, and By. The table lists three dispensing events for 2007.

Disp	Drug Name	Qty	Directions	Doc	Rpt	Dp	\$	By
19/07 2007	SPIRIVA INH-CAP 18mcg	30	Inhale the contents of ONE capsule using inhale	WATM	5	1	29.50	GM 7406
19/07 2007	CARDIZEM CD SR-CAP 240mg 30	30	Swallow whole ONE capsule daily *Do NOT st	WATM	5	1	32.06	GM 7407
19/07 2007	PRAVACHOL TAB 20mg	30	Take ONE tablet at night	WATM	1	1	31.19	GM 7408

At the bottom of the window are "Close" and "Send to Patient" buttons.

In-house testing of the MedeMine-for-COPD program's identification criteria found that more persistent patients would be identified than would be required. To minimise the cost of over-recruiting (due to the cost associated with patient incentives), MedeMine-for-COPD was programmed to include a maximum of ten persistent patients per pharmacy. Upon running the MedeMine-for-COPD program, persistent patients were ranked by the date of first tiotropium dispensing, and after the ten most recent dates, the rest of the patients were automatically excluded. This specific algorithm ensured that the ten persistent patients included received their first supply of tiotropium most recently, as they were more likely to remember details about their original diagnosis and prescription.

5.2.3 Sample size

The aim was to recruit at least 20 pharmacies from the South, North and North-West regions of Tasmania. Sample data from two pharmacies of small-average size suggested that at least four persistent patients and four non-persistent patients would be identified from each pharmacy. This would give a potential sample size of approximately 160 patients across all sites. It was envisaged that an approximate 50% response rate to the

invitation to participate, giving a sample size of 80 patients across the sites (40 persistent patients and 40 non-persistent patients).

The proposed sample size reflects the mix of quantitative and qualitative research objectives. A larger sample size was required for quantitative purposes. The generally accepted rule of thumb is that a minimum of 20 usable responses per cell is required for the type of multivariate statistical analysis planned for this research. Clearly larger sample sizes are required to conduct quantitative analysis with rigour and to be able to cut the data on multiple dimensions (age, gender, smoking status, depression etc). Given that a smaller sample size would be required to provide sufficient qualitative insights, face-to-face interviews were conducted with only half the sample (i.e. $n = 40$), whereas the full sample will be used to collect quantitative data (i.e. $n = 80$). It was envisaged that a sufficient number of patients would be recruited for interviews until definite themes relating to persistence emerged.

5.2.4 Pharmacy recruitment

Community pharmacists throughout the Tasmania were informed about the study via telephone, and sent a letter (Appendix 28) and project synopsis (Appendix 29) informing them about the study and inviting them to participate if they were a current user of the Fred dispensing system. Pharmacists were required to fax an expression of interest form to the researchers, indicating whether they felt the study would be worthwhile and they had time to commit to participate (Appendix 30).

In order to thank pharmacists for their assistance with the study, they were offered a \$500 honorarium to compensate for their time and professional input.

5.2.5 Installation and running the MedeMine COPD program

The data mining application was installed in the participating pharmacies and the pharmacists were instructed on its use and the study's procedures. Each pharmacy ran the software application and generated a list of patients identified as persistent or non-persistent with tiotropium.

The participating pharmacist examined the information for the patients and, using their professional judgement based on their knowledge of each patient, confirmed that it would be appropriate to send them an invitation letter. The pharmacists were encouraged to include all patients unless they met the pre-defined exclusion criteria.

- Patients who were nursing home residents were excluded because, in order to study the drivers and barriers of persistence, identified patients needed to be managing their own drug therapy;
- Pharmacists used their knowledge and experience with patients to assess whether receiving an invitation letter might have overly alarmed any patients. Such exclusions were deemed necessary to avoid causing undue distress to some patients;
- Because the study involved the completion of questionnaires and interviews, patients with impaired cognition or who would be too confused were excluded;
- Deceased patients were excluded; and
- Patients who were aged less than 40 years of age were excluded so that the identified patients were more likely to have a diagnosis of COPD rather than asthma.

The exclusion criteria were listed in a drop down menu, as shown in Figure 40.

Figure 40. Excluding patients in MedeMine-for-COPD

The screenshot shows a software window titled "Viewing Spiriva trial for A PATIENT". At the top, there is a text field containing "A PATIENT" and a dropdown menu labeled "Reason not included". The dropdown menu is open, displaying a list of exclusion reasons: "Too confused", "Deceased", "Patient is younger than 40 years old", "Nursing Home Resident", "May cause undue distress", and "Other ...". Below the dropdown, a table displays patient data. The table has two rows of data. The first row shows the date "19/07", medication "SPIRIVA INH-CAP", dosage "30", instruction "Inhale the contents of", unit "WATM", quantity "5", weight "1", and amount "29.50 GM". The second row shows the date "2007", medication "18mcg", dosage "ONE capsule using inhale", and amount "7406". At the bottom of the window, there are two buttons: "Close" and "Send to Patient".

19/07	SPIRIVA INH-CAP	30	Inhale the contents of	WATM	5	1	29.50 GM
2007	18mcg		ONE capsule using inhale				7406

In addition, if the pharmacist did not believe the patient was eligible to participate for any other reason, they could select 'other...' and type the reason. Due to the possibility

of patients receiving tiotropium from other pharmacies, pharmacists were also encouraged to exclude patients who were not regular clients of their pharmacy.

Once a patient was deemed eligible to be included in the study, a personalised invitation letter (Appendix 31) and consent form (Appendix 32) were printed directly from the MedeMine-for-COPD program. These, in addition to a generic patient information sheet (Appendix 33) and postage paid envelope, were mailed to all eligible patients.

When the process was complete and the MedeMine-for-COPD program was closed, the de-identified and encrypted dispensing information was automatically sent via the Internet to a secure server at the University of Tasmania.

5.2.6 Patient questionnaires

Patients who sent a signed consent to the University of Tasmania were subsequently sent a letter (Appendix 34) and patient questionnaire (Appendix 35). The patient questionnaire was composed of 20 questions, and included general non-validated questions relating to exposure to risk factors and a combination of validated questionnaires:

- The St. George's Respiratory Questionnaire;⁵⁸⁰
- The Brief Illness Perception Questionnaire;⁵⁸¹
- The Beliefs about Medicines Questionnaire;⁵⁸²
- The Hospital Anxiety and Depression Scale;⁵⁸³ and
- The Tool for Adherence Behaviour Screening.³⁴⁸

Patients who returned a completed questionnaire were sent a \$50 gift voucher.

5.2.6.1 St. George's Respiratory Questionnaire

The St. George's Respiratory Questionnaire (SGRQ) is a disease-specific measure of health status for use in COPD. It is a standardised self-administered questionnaire divided into three subscales: Symptoms (8 items), Activity (16 items) and Impacts (26 items).^{580,584} The Symptoms component is designed to assess patients' perception of their recent respiratory problems. The Activity component measures disturbances to patients' daily physical activity. The Impacts component covers a wide range of disturbances of psychosocial function. For each subscale and for the overall

questionnaire, scores range from zero (no impairment) to 100 (maximum impairment). Questions 4 through to 17 of the patient questionnaire, as displayed in Appendix 35, assessed all the items of the SGRQ. Questions 4 to 8 assessed symptoms, questions 11 and 15 assessed activity limitation and questions 9 to 10, 12 to 14, and 16 to 17 assessed psychosocial impacts.

There is now a wide body of published data on the SGRQ in COPD patients, including numerous large clinical trials of pharmacological⁵⁸⁵⁻⁵⁹⁰ and non-pharmacological^{498,591} interventions. There is extensive literature that points to the validity of the SGRQ, both from cross-sectional studies between patients, and longitudinally within patients.⁵⁹² The threshold for a clinically significant difference between groups of patients and for changes within groups of patients is four units.⁵⁹³

5.2.6.2 Brief Illness Perception Questionnaire

The Brief Illness perception questionnaire (IPQ) is a validated method for assessing cognitive representations of illness.^{581,594} The Brief IPQ, covered in question 18 of the patient questionnaire in Appendix 35, contains eight items, which are rated using a zero-to-ten response scale. Five of the items assessed cognitive illness representations (consequences [18a], timeline [18b], personal control [18c], treatment control [18d and identity [18e]), two of the items assessed emotional representations (concern [18f] and emotions [18h] and one item assessed illness comprehensibility (18g). Because the brief IPQ is not disease-specific, the authors recommend replacing the word ‘illness’ with the name of the particular illness that is being examined.⁵⁸¹ In this case, ‘respiratory condition’ was used.

5.2.6.3 Beliefs about Medicines Questionnaire

The Beliefs about Medicines Questionnaire (BMQ) is a validated method for assessing cognitive representations of medication.⁵⁸² The BMQ comprises two sections, which can be used in combination or separately. The BMQ-Specific assesses representations of medication prescribed for personal use and the BMQ-General assesses beliefs about medicines in general. Because not all patients recruited to this study would be taking the same medication, the BMQ-general was chosen, and is covered in question 19 of the patient questionnaire in Appendix 35. The BMQ-General comprises a General Harm scale (questions 19b, 19c, 19e and 19f of the patient questionnaire) and a General Overuse scale (19a 19d, 19g and 19h of the patient questionnaire). The General Harm

scale assesses beliefs about the intrinsic nature of medicines and the degree to which they are perceived as harmful and addictive poisons that should not be taken continuously. The General Overuse scale assesses beliefs about the use of medicines and whether doctors overprescribe them. Scores for each scale were summed, resulting in a range from 4 to 20. Higher scores indicate a more negative orientation towards medicines in general.

5.2.6.4 Tool for Adherence Screening Behaviour

The Tool for Adherence Behaviour Screening (TABS) is a validated scale that screens both intentional and unintentional non-adherence to pharmacological and non-pharmacological disease management.³⁴⁸ The TABS, covered in question 20 of the patient questionnaire in Appendix 35, measures adherent and non-adherent behaviour on five-point Likert-type scales. Questions 20b, 20c, 20d and 20e assess adherent behaviour, and questions 20a, 20f, 20g and 20h assess non-adherent behaviour, with higher scores indicating higher degrees of adherent and non-adherent behaviour. The items used in the TABS were developed based on common adherence issues experienced by a sample of chronically ill patients and cover domains, judged by experts, to be important in adherence screening.³⁴⁸

5.2.6.5 Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) was designed to provide a simple yet reliable tool for use in medical practice.⁵⁸³ The term ‘hospital’ in its title suggests that is only valid in such a setting but many studies conducted throughout the world have confirmed that it is valid when used in community settings.⁵⁹⁵ The HADS, covered in question 21 of the patient questionnaire in Appendix 35, contains 14 statements describing symptoms of depression and anxiety. Responses options for each question range from zero to three and ask patients about their agreement with the statements or how often they apply. There are seven statements for each depression (questions 21b, 21d, 21f, 21h, 21j, 21l and 21n of the patient questionnaire) and anxiety (questions 21a, 21c, 21e, 21g, 21i, 21k, 21m). Domain scores range from zero to 21 and following the standard convention scores ≥ 11 indicate a probable clinical diagnosis of depression or anxiety.⁵⁸³

5.2.7 Patient interviews

Approximately half of the consenting patients were invited to participate in qualitative face-to-face interviews. The interviews were conducted in patients' homes, which was not only more comfortable for patients, but also allowed the interviewers to observe the environment that the patients live in and to either test or more fully explore patient routines in taking their medication. With the patients' permission, each interview was digitally voice recorded. All interviewees received a cash gratuity of \$70.

The interviews addressed patient characteristics, diagnosis, treatment choice, day-to-day management and persistence with therapy. The face-to-face discussion guide, as displayed in Appendix 36, incorporated all of the qualitative objectives under each of the following discussion points:

- Understand rational and emotional thoughts and feelings towards patients' condition and health;
- Determine what part symptoms play in the decision to go to a doctor;
- Understand why diagnosed patients may not be filling prescriptions and determine the barriers to filling prescriptions;
- If patients have stopped taking their medication, determine what encouraged them to stop;
- Determine if patients use the medication on a symptomatic or regular basis; and
- Determine what would encourage patients to take their medication as prescribed and whether there are any other medications they are compliant with.

Whilst utilising a semi-structured interview outline, the emphasis and technical complexity of each interview naturally varied according to the expertise and perspective of the interviewee concerned. Best practice indicated that the interviewer was unknown to the participants and care was taken to ensure that the interview procedure was consistent during the study period.

In addition, to account for the possibility of patients receiving tiotropium from other pharmacies but being identified by the MedeMine-for-COPD program as non-persistent, self-reported persistence was determined in the qualitative interviews. The remainder of

non-persistent patients who had not been interviewed were screened via telephone interviews to determine self-reported persistence.

5.2.8 Handling of data and statistical analysis

All quantitative variables were collated and entered into a statistical software package, Statview 5.01 for Windows (Abacus Concepts Inc, Berkeley, California, USA). Categorical demographic variables of the persistent patients were compared to the non-persistent patients using the Chi Square test or Fisher's Exact test. The Fisher's Exact test was used when at least one of the variables had less than five patients or events. The Mann-Whitney *U* test was used to compare responses to individual questionnaire items and the questionnaires scores between persistent and non-persistent patients. Multivariate logistic regression models were then performed on items with significant univariate differences between the groups to identify the independent predictors of persistence. Spearman's correlation coefficients were calculated to determine the relationship between the significant independent predictors. A significance level of $P < 0.05$ was used for all statistical procedures.

Each interview was digitally voice recorded and transcribed verbatim. The qualitative analysis encompassed the three general phases of familiarisation, data reduction, and interpretation. The familiarisation process involved the researchers reading and listening to the data, to familiarise themselves with the data and to identify the various themes that emerged. Each topic in the interview schedule was analysed, identifying similarities or differences in participant responses and summarising key points (data reduction). The methodology utilised to analyse the transcripts was content analysis, which followed the principles of 'grounded theory', whereby concepts, categories and themes were identified and developed as they emerged from the interviews and any observational data.⁵⁹⁶

Interviewed and non-interviewed patients were analysed for differences in demographics, dispensing data, SGRQ scores and Anxiety and Depression scores.

5.2.9 Ethical approval and trial registration

Ethical approval was received from the Tasmanian Health and Medical Human Research Ethics Committee (ethics reference number H9842). The study was registered

with the Australian New Zealand Clinical Trial Registry (registration number ACTRN12608000120370).

5.3 Results

5.3.1 Recruitment of participants

5.3.1.1 Pharmacist participation

A total of 44 Tasmanian pharmacies were invited to participate in the study by telephone and mail. Table 57 displays the responses of pharmacists by the expression of interest form and follow-up telephone calls.

Table 57. Pharmacists' willingness to participate

Response	Number of pharmacies (n = 44)
Use the Fred dispensing system and willing to participate	37 (84.1%)
Do not use the Fred dispensing system	2 (4.5%)
Use the Fred dispensing system, but not able to participate	5 (11.4%)

Of the 37 pharmacies that agreed to participate in the study, one (2.7%) pharmacy was excluded due to failure of the MedeMine-for-COPD installation. Of the 36 pharmacies that participated in the study, 26 (72.2%) were classed as metropolitan and 10 (27.8%) were classed as rural.

5.3.1.2 Identification of patients

The MedeMine-for-COPD program identified a total of 1,291 patients from 36 pharmacies. Of these patients, 728 (56.4%) were identified as 'persistent' and 563 (43.6%) were identified as 'non-persistent.' Of the non-persistent patients, 266 (47.2%) received their last supply of tiotropium in the past six months, and 297 (52.8%) received their last supply of tiotropium in the past 7-12 months.

Table 58 displays the number of patients identified by each pharmacy. An average of 36 patients were identified in each pharmacy. Of these patients, an average of 20 (55.6%) patients were identified as persistent, and an average of 16 (44.4%) were identified as non-persistent.

There was a significant difference in the proportion of persistent and non-persistent patients identified in rural and metropolitan pharmacies. Of the 968 patients identified in metropolitan pharmacies, 516 (53.3%) were persistent and 452 (46.7%) were non-persistent, whereas of the 323 patients identified in rural pharmacies, 212 (65.6%) were persistent and 111 (34.4%) were non-persistent ($\chi^2 = 15.0$, $df = 1$, $P = 0.001$).

Table 58. Patients identified by each pharmacy

Pharmacy ID	Region	Patients identified* (n = 1,291)	Persistent [†] (n = 728)	Non-persistent [†] (n = 1,126)		
				Total (n = 563)	Recent (n = 266)	Late (n = 279)
1	Metro	35 (2.7%)	15 (42.9%)	20 (57.1%)	13 (37.1%)	7 (20.0%)
2	Metro	15 (1.2%)	12 (80.0%)	3 (20.0%)	1 (6.7%)	2 (13.3%)
3	Rural	48 (3.7%)	33 (68.8%)	15 (31.3%)	11 (22.9%)	4 (8.3%)
4	Rural	23 (1.8%)	15 (65.2%)	8 (34.8%)	3 (13.0%)	5 (21.7%)
5	Metro	25 (1.9%)	14 (56.0%)	11 (44.0%)	5 (20.0%)	6 (24.0%)
6	Metro	27 (2.1%)	8 (29.6%)	19 (70.4%)	6 (22.2%)	13 (48.1%)
7	Rural	22 (1.7%)	14 (63.6%)	8 (36.4%)	7 (31.8%)	1 (4.5%)
8	Rural	39 (3.0%)	26 (66.7%)	13 (33.3%)	10 (25.6%)	3 (7.7%)
9	Metro	52 (4.0%)	17 (32.7%)	35 (67.3%)	20 (38.5%)	15 (28.8%)
10	Rural	23 (1.8%)	13 (56.5%)	10 (43.5%)	6 (26.1%)	4 (17.4%)
11	Metro	24 (1.9%)	10 (41.7%)	14 (58.3%)	8 (33.3%)	6 (25.0%)
12	Metro	33 (2.6%)	26 (78.8%)	7 (21.2%)	4 (12.1%)	3 (9.1%)
13	Metro	41 (3.2%)	31 (75.6%)	10 (24.4%)	7 (17.1%)	3 (7.3%)
14	Metro	65 (5.0%)	37 (56.9%)	28 (43.1%)	14 (21.5%)	14 (21.5%)
15	Metro	9 (0.7%)	1 (11.1%)	8 (88.9%)	3 (33.3%)	5 (55.6%)
16	Metro	28 (2.2%)	17 (60.7%)	11 (39.3%)	5 (17.9%)	6 (21.4%)
17	Metro	102 (7.9%)	50 (49.0%)	52 (51.0%)	23 (22.5%)	29 (28.4%)
18	Metro	50 (3.9%)	29 (58.0%)	21 (42.0%)	12 (24.0%)	9 (18.0%)
19	Metro	17 (1.3%)	15 (88.2%)	2 (11.8%)	0 (0.0%)	2 (11.8%)
20	Metro	26 (2.0%)	20 (76.9%)	6 (23.1%)	4 (15.4%)	2 (7.7%)
21	Metro	39 (3.0%)	29 (74.4%)	10 (25.6%)	5 (12.8%)	5 (12.8%)
22	Rural	18 (1.4%)	16 (88.9%)	2 (11.1%)	1 (5.6%)	1 (5.6%)
23	Metro	21 (1.5%)	16 (76.2%)	5 (23.8%)	2 (9.5%)	3 (14.3%)
24	Metro	33 (2.6%)	21 (63.6%)	12 (36.4%)	7 (21.2%)	5 (15.2%)
25	Metro	72 (5.6%)	27 (37.5%)	45 (62.5%)	18 (25.0%)	27 (37.5%)
26	Metro	83 (6.4%)	36 (43.4%)	47 (56.6%)	17 (20.5%)	30 (36.1%)
27	Metro	29 (2.3%)	18 (62.1%)	11 (37.9%)	4 (13.8%)	7 (24.1%)
28	Rural	35 (2.7%)	20 (57.1%)	15 (42.9%)	5 (14.3%)	10 (28.6%)
29	Rural	33 (2.6%)	21 (63.6%)	12 (36.4%)	6 (18.2%)	6 (18.2%)
30	Metro	24 (1.9%)	13 (54.2%)	11 (45.8%)	7 (29.2%)	4 (16.7%)
31	Metro	64 (5.0%)	29 (45.3%)	35 (54.7%)	11 (17.2%)	24 (37.5%)
32	Rural	74 (5.7%)	46 (62.2%)	28 (37.8%)	11 (14.9%)	17 (23.0%)
33	Rural	8 (0.6%)	8 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
34	Metro	7 (0.5%)	1 (14.3%)	6 (85.7%)	2 (28.6%)	4 (57.1%)
35	Metro	19 (1.5%)	14 (73.7%)	5 (26.3%)	2 (10.5%)	3 (15.8%)
36	Metro	28 (2.2%)	10 (35.7%)	18 (64.3%)	6 (21.4%)	12 (42.9%)

*Figures represent number (%) of total patients identified. [†]Figures represent number (%) of total patients identified in each pharmacy.

5.3.1.3 Patient exclusions

Of the 1,291 patients identified, 862 (66.8%) were excluded from the study, leaving 429 (33.2%) patients eligible to be invited to participate. Of the excluded patients, 489 (56.7%) were excluded automatically by the MedeMine-for-COPD program as being in excess of recruitment requirements, and 373 (43.3%) were excluded by pharmacists. There was a significant difference in the excluded proportion of persistent and non-persistent patients for the reasons ‘not a regular patient’ (0/53 [0.0%] versus 280/320 [87.5%], respectively; $\chi^2 = 702.4$, $df = 1$, $P < 0.0001$), ‘patient is deceased’ (0/53 [0.0%] versus 10/320 [3.1%], respectively; $\chi^2 = 17.1$, $df = 1$, $P < 0.0001$) and ‘patient is younger than 40 years of age’ (0/542 [0.0%] versus 4/320 [1.3%], $\chi^2 = 6.8$, $df = 1$, $P < 0.05$). Table 59 displays the reasons for patient exclusion by pharmacists, with the assistance of a researcher.

Table 59. Reasons for patient exclusion by pharmacists*

Reason for exclusion	Patients excluded (n = 373)	Persistent (n = 53)	Non-persistent (n = 320)	<i>P</i>
Not a regular patient	280 (75.1%)	0 (0.0%)	280 (87.5%)	< 0.0001
Nursing home resident	47 (12.6%)	33 (62.3%)	14 (4.4%)	0.28
May cause undue distress to patient	12 (3.2%)	7 (13.2%)	5 (1.6%)	0.74
Patient is too confused	12 (3.2%)	8 (15.1%)	4 (1.3%)	> 0.99
Patient is deceased	10 (2.7%)	0 (0.0%)	10 (3.1%)	< 0.0001
Patient has a language barrier	5 (1.3%)	2 (3.8%)	3 (0.9%)	0.37
Patient is younger than 40 years old	4 (1.1%)	0 (0.0%)	4 (1.3%)	0.02
Patient is disabled	2 (0.5%)	2 (3.8%)	0 (0.0%)	0.53
Patient is illiterate	1 (0.3%)	1 (1.9%)	0 (0.0%)	> 0.99

*Figures represent number (%) of excluded patients.

Table 60 displays the number of patients excluded per pharmacy. All the identified patients were excluded in four of the pharmacies. Of the 36 pharmacies that ran the MedeMine-for-COPD program, 32 (88.9%) were left with patients who were eligible to be invited to participate.

Table 60. Patients excluded per pharmacy*

Pharmacy ID	Persistent			Non-persistent		
	Identified (n = 728)	Included (n = 186)	Excluded (n = 542)	Identified (n = 563)	Included (n = 243)	Excluded (n = 320)
1	15	5 (33.3%)	10 (66.7%)	20	16 (80.0%)	14 (20.0%)
2	12	9 (75.0%)	3 (25.0%)	3	3 (100.0%)	0 (0.0%)
3	33	9 (27.3%)	24 (72.7%)	15	7 (46.7%)	8 (53.3%)
4	15	9 (60.0%)	6 (40.0%)	8	7 (87.5%)	1 (12.5%)
5	14	8 (57.1%)	6 (42.9%)	11	8 (72.7%)	3 (27.3%)
6	8	8 (100.0%)	0 (0.0%)	19	0 (0.0%)	19 (100.0%)
7	14	9 (64.3%)	5 (35.7%)	8	6 (75.0%)	2 (25.0%)
8	26	10 (38.5%)	16 (61.5%)	13	9 (69.2%)	4 (30.8%)
9	17	8 (47.1%)	9 (52.9%)	35	27 (77.1%)	8 (22.9%)
10	13	10 (76.9%)	3 (23.1%)	10	7 (70.0%)	3 (30.0%)
11	10	8 (80.0%)	2 (20.0%)	14	3 (21.4%)	11 (78.6%)
12	26	8 (30.8%)	18 (69.2%)	7	3 (42.9%)	4 (57.1%)
13	31	9 (29.0%)	22 (71.0%)	10	5 (50.0%)	5 (50.0%)
14	37	8 (21.6%)	29 (78.4%)	28	10 (35.7%)	18 (64.3%)
15	1	0 (0.0%)	1 (100.0%)	8	5 (62.5%)	3 (37.5%)
16	17	4 (23.5%)	13 (76.5%)	11	5 (45.5%)	6 (54.5%)
17	50	8 (16.0%)	42 (84.0%)	52	22 (42.3%)	30 (57.7%)
18	29	8 (27.6%)	21 (72.4%)	21	12 (57.1%)	9 (42.9%)
19	15	10 (66.7%)	5 (33.3%)	2	2 (100.0%)	0 (0.0%)
20	20	8 (40.0%)	12 (60.0%)	6	6 (100.0%)	0 (0.0%)
21	29	8 (27.6%)	21 (72.4%)	10	6 (60.0%)	4 (40.0%)
22	16	8 (50.0%)	8 (50.0%)	2	2 (100.0%)	0 (0.0%)
23	16	3 (18.8%)	13 (81.3%)	5	3 (60.0%)	2 (40.0%)
24	21	6 (28.6%)	15 (71.4%)	12	3 (25.0%)	9 (75.0%)
25	27	5 (18.5%)	22 (81.5%)	45	41 (91.1%)	4 (8.9%)
26 [†]	36	0 (0.0%)	36 (100.0%)	47	4 (8.5%)	43 (91.5%)
27 [†]	18	0 (0.0%)	18 (100.0%)	11	2 (18.2%)	9 (81.8%)
28 [†]	20	0 (0.0%)	20 (100.0%)	15	3 (20.0%)	12 (80.0%)
29 [†]	21	0 (0.0%)	21 (100.0%)	12	4 (33.3%)	8 (66.7%)
30 [†]	13	0 (0.0%)	13 (100.0%)	11	4 (36.4%)	7 (63.6%)
31 [†]	29	0 (0.0%)	29 (100.0%)	35	7 (20.0%)	28 (80.0%)
32 [†]	46	0 (0.0%)	46 (100.0%)	28	11 (39.3%)	17 (60.7%)
33 [†]	8	0 (0.0%)	8 (100.0%)	0	0 (0.0%)	0 (0.0%)
34 [†]	1	0 (0.0%)	1 (100.0%)	6	0 (0.0%)	6 (100.0%)
35 [†]	14	0 (0.0%)	14 (100.0%)	5	0 (0.0%)	5 (100.0%)
36 [†]	10	0 (0.0%)	10 (100.0%)	18	0 (0.0%)	18 (100.0%)

*Figures represent number (%) of patients persistent or non-persistent identified in each pharmacy.

[†]Pharmacies recruited at a later date to increase numbers of non-persistent patients; all persistent patients were excluded from these pharmacies.

5.3.1.4 Patient participation

Of the 429 patients who were sent invitations to participate in the study, 136 (31.7%) agreed to participate and sent signed consent forms to the researchers. A significantly higher proportion of persistent patients agreed to participate than non-persistent patients (74/186, [39.8%] versus 62/243 [25.5%], respectively; $\chi^2 = 9.9$, $df = 1$, $P < 0.01$). Of the consenting patients, 129 (94.9%) returned the patient questionnaires. Table 61 summarises the patient response rates.

Table 61. Patient response rates*

Mail-out description		All patients	Persistent	Non-persistent	P
1	Sent invitation to participate by pharmacist	429	186	243	
	Returned consent form to researchers	136 (31.7%)	74 (39.8%)	62 (25.5%)	0.002
2	Sent patient questionnaire by researchers	136	74	62	
	Returned patient questionnaire to researchers	129 (94.9%)	71 (95.9%)	58 (93.5%)	0.53

*Figures represent number sent and number (%) returned.

5.3.2 Quantitative analyses

5.3.2.1 Consenting patients' demographics and dispensing data

Table 62 displays the demographic parameters and dispensing data for all consenting patients. No significant differences between the persistent and non-persistent patients were observed in terms of age, gender or region of pharmacy.

RM-experienced patients were significantly more likely to be persistent with tiotropium (35/50 [70.0%] were persistent, compared with only 39/86 [45.3%] of the RM-naïve patients; $\chi^2 = 7.7$, $df = 1$, $P < 0.01$).

Patients who were dispensed medication for co-morbidities in the past 12 months were also significantly more likely to be persistent with tiotropium (69/117 [59.0%] were persistent, compared with only 5/19 [26.3%] of the patients who were not dispensed medications for co-morbidities; $\chi^2 = 7.0$, $df = 1$, $P < 0.01$).

There was no significant difference in the proportion of persistent and non-persistent patients who had received antidepressant medications or who had received prescriptions at the concession rate in the past 12 months.

Table 62. Patient demographics and dispensing data

Parameter	All patients* (n = 136)	Persistent [†] (n = 74)	Non-persistent [†] (n = 62)	P
Age in years (mean ± SD)	68.7 ± 11.2	69.8 ± 9.4	67.3 ± 13.0	0.20
Gender				
Male	69 (50.7%)	40 (58.0%)	29 (42.0%)	0.40
Female	67 (49.3%)	34 (50.7%)	33 (49.3%)	
Region of pharmacy				
Metro	94 (69.1%)	49 (52.1%)	45 (47.9%)	0.42
Rural	42 (30.9%)	25 (59.5%)	17 (40.5%)	
RM status				
RM-experienced	50 (36.8%)	35 (70.0%)	15 (30.0%)	0.005
RM-naïve	86 (63.2%)	39 (45.3%)	47 (54.7%)	
Medication dispensed for co-morbidities [‡]				
Yes	117 (86.0%)	69 (59.0%)	48 (41.0%)	0.007
No	19 (14.0%)	5 (26.3%)	14 (73.7%)	
Antidepressant dispensed [‡]				
Yes	35 (25.7%)	19 (54.3%)	16 (45.7%)	0.99
No	101 (74.3%)	55 (54.5%)	46 (45.5%)	
Prescriptions dispensed at concession rate [‡]				
Yes	124 (91.2%)	68 (54.8%)	56 (45.2%)	0.75
No	12 (8.8%)	6 (50.0%)	6 (50.0%)	

*Figures represent number (%) of total patients. [†]Figures represent number (%) of patients in each parameter. [‡]In the 12 months preceding identification.

Consenting patients were representative of non-consenting patients in terms of all dispensing data parameters, with no significant differences demonstrated between the consenting and non-consenting patients in pharmacy region, RM status, whether medications had been dispensed for co-morbidities, whether antidepressants had been dispensed or whether prescriptions had been dispensed at the concessional rate in the past year (Table 63).

Table 63. Comparison of consenting and declining patients' dispensing data

Parameter	All patients*		Persistent [†]		Non-persistent [†]	
	Consented (n = 136)	Declined [‡] (n = 293)	Consented (n = 74)	Declined (n = 112)	Consented (n = 62)	Declined (n = 181)
<i>Region of pharmacy</i>						
Metro	94 (69.1%)	224 (76.5%)	49 (52.1%)	82 (36.7%)	45 (47.9%)	142 (63.4%)
Rural	42 (30.9%)	69 (23.5%)	25 (59.5%)	30 (43.5%)	17 (40.5%)	39 (56.5%)
<i>P</i> value	0.11		0.31		0.34	
<i>RM status</i>						
Naive	86 (63.2%)	204 (69.6%)	39 (45.3%)	61 (29.9%)	47 (54.7%)	143 (70.1%)
Experienced	50 (36.8%)	87 (29.7%)	35 (70.0%)	51 (58.6%)	15 (30.0%)	36 (41.4%)
<i>P</i> value	0.16		0.81		0.50	
<i>Medication dispensed for co-morbidities[§]</i>						
Yes	117 (86.0%)	254 (86.7%)	69 (59.0%)	106 (41.7%)	48 (41.0%)	148 (58.3%)
No	19 (14.0%)	37 (12.6%)	5 (26.3%)	6 (16.2%)	14 (73.7%)	31 (83.8%)
<i>P</i> value	0.72		0.69		0.36	
<i>Antidepressant dispensed[§]</i>						
Yes	35 (25.7%)	70 (23.9%)	19 (54.3%)	31 (44.3%)	16 (45.7%)	39 (55.7%)
No	101 (74.3%)	221 (75.4%)	55 (54.5%)	81 (36.7%)	46 (45.5%)	140 (63.3%)
<i>P</i> value	0.71		0.76		0.52	
<i>Prescriptions dispensed at concession rate[§]</i>						
Yes	124 (91.2%)	261 (54.9%)	68 (54.8%)	105 (40.2%)	56 (45.2%)	156 (59.8%)
No	12 (8.8%)	30 (10.2%)	6 (50.0%)	7 (23.3%)	6 (50.0%)	23 (76.7%)
<i>P</i> value	0.63		0.63		0.51	

*Figures represent number (%) of patients. [†]Figures represent number (%) of patients in each parameter.

[‡]Percentages may not add up to 100 due to the unavailability of two patients' dispensing data. [§]In the 12 months preceding identification.

5.3.2.2 Exposure to COPD risk factors

Table 64 displays the exposure of patients to COPD risk factors. No significant differences between the persistent and non-persistent patients were observed in terms of previous work exposure to dust, gas or chemical fumes, current exposure to passive cigarette smoke at home, current smoking status, number of cigarettes smoked per day or pack years.

The majority of all patients (57.4%) had previously worked for a year or more in a job that regularly exposed them to dust, gas or chemical fumes. The majority of all patients (82.2%) had been regular smokers in the past, although only 19.4% were still smokers

(which skewed the current average number of cigarettes smoked per day amongst all patients to zero), and the majority (81.4%) currently lived in smoke-free homes.

Table 64. Exposure to COPD risk factors*

Risk factor	All patients (n = 129)	Persistent (n = 71)	Non-persistent (n = 58)	P
Work exposure to dust, gas or chemical fumes [†]				
Yes	74 (57.4%)	39 (52.7%)	35 (47.3%)	0.54
No	55 (42.6%)	32 (58.2%)	23 (41.8%)	
Current home exposure				
People frequently smoke in the house	11 (8.5%)	7 (63.6%)	4 (36.4%)	0.16
People occasionally smoke in the house	13 (10.1%)	4 (30.8%)	9 (69.2%)	
My home is smoke free	105 (81.4%)	60 (57.1%)	45 (42.9%)	
Ever regularly smoked				
Yes	106 (82.2%)	58 (54.7%)	48 (45.3%)	0.71
No	22 (17.2%)	13 (59.1%)	9 (40.9%)	
Current smoker				
Yes	25 (19.4%)	11 (44.0%)	14 (56.0%)	0.22
No	104 (80.6%)	60 (57.7%)	44 (42.3%)	
Current number of cigarettes smoked per day				
All patients	0.0 (0.0 - 0.0)	0.0 (0.0-0.0)	0.0 (0.0 - 0.0)	0.42
Current smokers	18.8 (11.3 - 30.0)	15.0 (10.6 - 27.5)	25.0 (13.8 - 30.0)	0.64
Pack years	32.3 (11.3 - 49.8)	33.0 (6.0 - 49.0)	32.3 (13.9 - 51.7)	0.89

*Figures represent number (%) of all patients or median (inter-quartile range). Percentages may not add up to 100 due to blank responses. [†]Exposure for a year or more.

5.3.2.3 Respiratory-specific health status

Table 65 displays the component scores and total score for the St. George's Respiratory Questionnaire. No statistically significant differences between the persistent and non-persistent patients' scores were observed. However, dissimilarities between the Impacts score for persistent and non-persistent patients exceeded the threshold for a clinically significant difference of four units,⁵⁹³ with non-persistent patients displaying a higher degree of impairment.

Table 65. St. George's Respiratory Questionnaire scores*

Component	All patients (n = 129)	Persistent (n = 71)	Non-persistent (n = 58)	<i>P</i>
Symptoms	63.2 (47.8 - 79.3)	63.3 (49.0 - 78.3)	62.7 (45.2 - 83.6)	> 0.99
Activity	66.3 (49.6 - 85.9)	66.2 (52.0 - 85.9)	69.3 (47.7 - 85.9)	0.90
Impacts	36.4 (21.9 - 51.5)	33.3 (18.9 - 49.7)	40.2 (24.1 - 52.4)	0.19
Total	51.9 (37.1 - 64.7)	50.2 (33.7 - 62.0)	54.0 (38.7 - 66.9)	0.43

*Figures represent median (inter-quartile range) score; higher scores indicate higher degrees of impairment.

5.3.2.4 Illness perception

Table 66 displays the component scores for the Illness Perception Questionnaire. Persistent patients had significantly higher scores for the item “how much do you think your treatment can help your respiratory condition?” ($U = 1613.0$, $Z = 2.1$, $P < 0.05$). There was a non-significant trend for persistent patients to have higher scores on the item “how much control do you feel you have over your respiratory condition?” ($U = 1600.5$, $Z = 1.9$, $P = 0.06$). No other significant differences in illness perception were observed.

Table 66. Illness Perception Questionnaire scores*

Item	All patients (n = 129)	Persistent (n = 71)	Non-persistent (n = 58)	P
How much does your respiratory condition affect your life? [†]	5.0 (3.0 - 8.0)	6.0 (3.0 - 8.0)	5.0 (3.0 - 8.0)	0.42
How long do you think your respiratory condition will continue? [‡]	10.0 (10.0 - 10.0)	10.0 (10.0 - 10.0)	10.0 (9.0 - 10.0)	0.26
How much control do you feel you have over your respiratory condition? [§]	6.0 (4.0 - 8.0)	7.0 (5.0 - 8.0)	5.0 (2.0 - 7.0)	0.06
How much do you think your treatment can help your respiratory condition? [¶]	8.0 (5.0 - 10.0)	8.0 (6.0 - 10.0)	7.0 (4.0 - 10.0)	0.04
How much do you experience symptoms from your respiratory condition? ^{††}	6.0 (3.8 - 8.0)	6.0 (4.0 - 8.0)	5.5 (3.0 - 8.0)	0.58
How concerned are you about your respiratory condition? ^{‡‡}	8.0 (5.0 - 10.0)	8.0 (5.0 - 10.0)	8.0 (5.0 - 10.0)	0.88
How well do you feel you understand your respiratory condition? ^{§§}	10.0 (6.0 - 10.0)	10.0 (6.0 - 10.0)	10.0 (6.0 - 10.0)	0.97
How much does your respiratory condition affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?) ^{¶¶}	6.0 (2.0 - 8.0)	6.0 (2.0 - 8.0)	6.0 (1.0 - 8.0)	0.79

*Figures represent median (inter-quartile range) score. [†]0 = no affect at all; 10 = severely affects my life. [‡]0 = a very short time; 10 = forever. [§]0 = absolutely no control; 10 = extreme amount of control. [¶]0 = not at all; 10 = extremely helpful. ^{††}0 = no symptoms at all; 10 = many severe symptoms. ^{‡‡}0 = not at all concerned; 10 = extremely concerned. ^{§§}0 = don't understand at all; 10 = understand very clearly. ^{¶¶}0 = not at all affected emotionally; 10 = extremely effected emotionally.

5.3.2.5 Beliefs about medicines

Non-persistent patients had significantly higher scores for the item “medicines do more harm than good” ($U = 1433.5$, $Z = 2.8$, $P < 0.01$) from the Beliefs about Medicines Questionnaire, as displayed in Table 67. There was a non-significant trend for non-persistent patients to have higher overall Harm score ($U = 1647.5$, $Z = 1.8$, $P = 0.07$). No other significant differences were observed.

Table 67. Beliefs about Medicines Questionnaires scores*

Item	All patients (n = 129)	Persistent (n = 71)	Non-persistent (n = 58)	P
<i>Overuse items</i>				
Doctors prescribe too many medicines	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	0.68
Natural remedies are safer than medicines	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	3.0 (2.0 - 3.0)	0.14
Doctors place too much trust on medicines	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	2.0 (2.0 - 4.0)	0.11
If doctors had more time with patients they would prescribe fewer medicines	3.0 (2.0 - 4.0)	3.0 (2.0 - 3.0)	3.0 (2.0 - 4.0)	0.12
<i>Harm items</i>				
People who take medicines should stop their treatment for a while every now and again	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)	0.10
Most medicines are addictive	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	0.54
Medicines do more harm than good	2.0 (1.0 - 2.0)	2.0 (1.0 - 2.0)	2.0 (2.0 - 3.0)	0.005
All medicines are poisons	2.0 (1.0 - 2.5)	2.0 (1.0 - 2.0)	2.0 (1.0 - 3.0)	> 0.99
<i>Overuse score</i>	10.0 (8.0 - 12.0)	10.0 (8.0 - 12.0)	11.0 (8.0 - 13.3)	0.14
<i>Harm score</i>	8.0 (7.0 - 10.0)	8.0 (7.0 - 9.0)	9.0 (7.0 - 11.3)	0.07

*Figures represent median (inter-quartile range) score; 1 = strongly disagree; 5 = strongly agree.

5.3.2.6 Medication adherence behaviour

As displayed in Table 68, persistent patients had significantly higher scores than non-persistent patients on two of the adherence items (“I have strict routines for using my regular respiratory medications” [$U = 1087.0$, $Z = 3.6$, $P < 0.001$] and “I keep my respiratory medications close to where I need to use them” [$U = 1417.5$, $Z = 2.2$, $P < 0.05$]). Non-persistent patients had significantly higher scores than persistent patients on three of the non-adherence items (“I get confused about my respiratory medications” [$U = 1439.0$, $Z = 2.1$, $P < 0.05$], “I vary my recommended management depending on how I am feeling” [$U = 1269.0$, $Z = 2.7$, $P < 0.01$] and “I put up with my respiratory problems before taking any action” [$U = 1181.0$, $Z = 3.4$, $P < 0.001$]).

Persistent patients had significantly higher total adherence scores, and significantly lower total non-adherence scores, than non-persistent patients ($U = 1231.5$, $Z = 2.7$, $P < 0.01$ and $U = 1238.0$, $Z = 3.1$, $P < 0.01$, respectively).

Table 68. Medication adherence items and scores*

Item	All patients (n = 129)	Persistent (n = 71)	Non-persistent (n = 58)	P
<i>Adherence items</i>				
I have strict routines for using my respiratory medications	5.0 (4.5 - 5.0)	5.0 (5.0 - 5.0)	5.0 (3.0 - 5.0)	0.0003
I keep my respiratory medications close to where I need to use them	5.0 (5.0 - 5.0)	5.0 (5.0 - 5.0)	5.0 (5.0 - 5.0)	0.03
I ensure I have enough respiratory medications so that I don't run out	5.0 (5.0 - 5.0)	5.0 (5.0 - 5.0)	5.0 (5.0 - 5.0)	0.21
I push myself to follow the instructions of my doctors	5.0 (3.0 - 5.0)	5.0 (3.3 - 5.0)	4.0 (3.0 - 5.0)	0.26
<i>Non-adherence items</i>				
I get confused about my respiratory medications	1.0 (1.0 - 2.0)	1.0 (1.0 - 1.5)	1.0 (1.0 - 2.0)	0.04
I make changes in the recommended management to suit my lifestyle	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)	0.62
I vary my recommended management depending on how I am feeling	2.0 (1.0 - 3.0)	1.0 (1.0 - 3.0)	3.0 (1.0 - 3.0)	0.005
I put up with my respiratory problems before taking any action	2.0 (1.0-3.0)	1.0 (1.0 - 3.0)	3.0 (2.0 - 4.0)	0.0007
<i>Adherence score</i>	19.0 (17.0 - 20.0)	20.0 (18.0 - 20.0)	17.0 (16.0 - 20.0)	0.007
<i>Non-adherence score</i>	8.0 (5.0 - 11.0)	7.0 (4.0 - 10.0)	10 (6.0 - 12.0)	0.002

*Figures represent median (inter-quartile range) score; 1 = never; 5 = always.

5.3.2.7 Anxiety and depression

No significant differences were observed in persistent and non-persistent patents' scores for the Hospital Anxiety and Depression Scale, as displayed in Table 69.

Table 69. Anxiety and depression items and scores*

Item	All patients (n = 129)	Persistent (n = 71)	Non-persistent (n = 58)	P
<i>Anxiety items</i>				
I feel tense or wound up	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)	0.84
I get a sort of frightened feeling as if something awful is about to happen	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)	0.37
Worrying thoughts go through my mind	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)	0.39
I can sit at ease and feel relaxed [†]	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (1.0 - 1.0)	0.50
I get a sort of frightened feeling like butterflies in the stomach	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.20
I feel restless as if I have to be on the move	1.0 (0.5 - 2.0)	1.0 (0.0 - 2.0)	1.0 (1.0 - 2.0)	0.33
I get sudden feelings of panic	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.90
<i>Depression items</i>				
I still enjoy the things I used to enjoy [†]	1.0 (1.0 - 1.0)	1.0 (1.0 - 1.8)	1.0 (1.0 - 2.0)	0.81
I can laugh and see the funny side of things [†]	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.56
I feel cheerful [†]	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.52
I feel as if I am slowed down	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)	0.40
I have lost interest in my appearance	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.64
I look forward with enjoyment to things [†]	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 2.0)	0.26
I can enjoy a good book or radio or TV program [†]	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 1.0)	0.29
<i>Anxiety score</i>	6.0 (3.3 - 10.0)	6.0 (3.0 - 10.0)	7.0 (4.0 - 10.0)	0.28
<i>Depression score</i>	5.0 (3.0 - 8.0)	5.0 (3.0 - 7.0)	6.0 (4.0 - 8.0)	0.24

*Figures represent median (inter-quartile range) score; 0 = no, not at all; 3 = yes, definitely. [†]Reverse-scored.

5.3.2.8 Multivariate analysis

When logistic regression was performed on persistence, a model comprising all of the significant ($P < 0.05$) variables from univariate analyses explained 30.8% variance in persistence. Low agreement with the statement “medicines do more harm than good” and high agreement with the statement “I have strict routines for using my respiratory medications” were found to be significant independent predictors for persistence, as displayed in Table 70. These two variables together explained 20.3% variance in persistence in the study population.

Table 70. Multivariate predictors of persistence

Predictor	χ^2	<i>P</i>
<i>Dispensing data</i>		
RM status	0.9	0.33
Medication dispensed for co-morbidities in the past 12 months	3.0	0.08
<i>Questionnaire items</i>		
How much do you think your treatment can help your respiratory condition?	1.2	0.27
Medicines do more harm than good*	7.0	0.008
I get confused about my respiratory medications	0.3	0.56
I have strict routines for using my respiratory medications*	10.2	0.001
I keep my respiratory medications close to where I need to use them	3.5	0.06
I vary my recommended management depending on how I am feeling	< 0.1	0.88
I put up with my respiratory problems before taking any action	1.1	0.29

*Significant independent predictor.

A significant negative correlation was demonstrated between the two independent predictors of persistence; patients who agreed that medicine do more harm than good were less likely to have strict routines for using their respiratory medications ($r_s = 0.2$, $P < 0.05$).

5.3.3 Qualitative analyses

5.3.3.1 Characteristics of interviewed patients

A convenience sample of 48 patients (33 persistent and 15 non-persistent) participated in face-to-face interviews. Table 71 displays the characteristics of the patients who were interviewed.

Table 71. Characteristics of interviewed patients

Parameter	All interviewed patients* (n = 48)	Persistent ^{†‡} (n = 33)	Non-persistent [†] (n = 15)
Age in years (mean \pm SD)	64.3 \pm 10.1	65.2 \pm 9.3	62.1 \pm 11.8
<i>Gender</i>			
Male	21 (43.8%)	14 (66.7%)	7 (33.3%)
Female	27 (56.3%)	19 (70.4%)	8 (29.6%)
<i>Region of pharmacy</i>			
Metro	25 (52.1%)	15 (60.0%)	10 (40.0%)
Rural	23 (47.9%)	18 (78.3%)	5 (21.7%)
<i>RM status</i>			
RM-experienced	22 (45.8%)	13 (59.1%)	9 (40.1%)
RM-naïve	26 (54.2%)	20 (76.9%)	6 (23.1%)

*Figures represent number (%) of patients. [†]Figures represent number (%) of patients in each parameter.

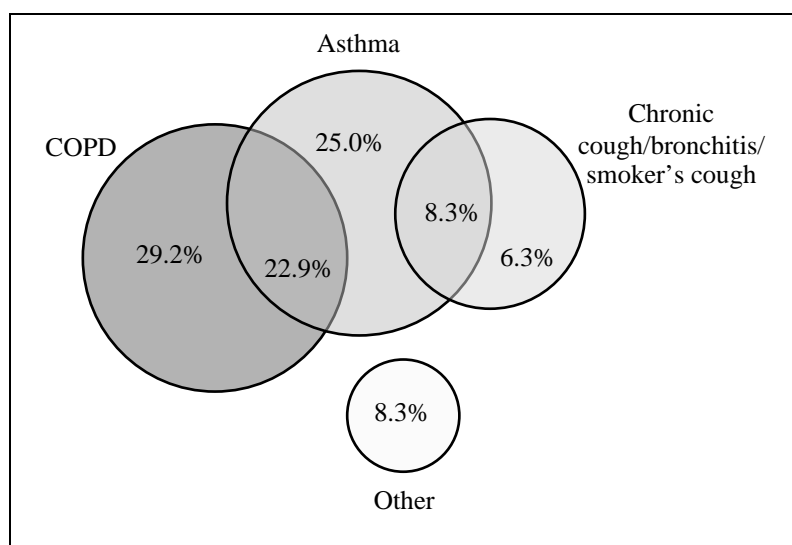
Table 72 displays the characteristics of the interviewed patients as compared to the rest of the consenting patients. Interviewed patients were significantly younger than the rest of the consenting patients (64.3 \pm 10.1 versus 71.2 \pm 11.0 years; $U = 1337.5$, $Z = 3.4$, $P < 0.001$), and a significantly greater proportion of interviewed patients were identified from rural pharmacies compared to the rest of the consenting patients (23/48 [47.9%] versus 19/88 [21.6%]; $\chi^2 = 10.1$, $df = 1$, $P < 0.01$). Interviewed patients were representative of the rest of the consenting patients in terms of gender, whether medications had been dispensed for co-morbidities, whether antidepressants had been dispensed or whether prescriptions had been dispensed at the concessional rate in the past year, smoking history, respiratory-specific quality of life and anxiety and depression scores.

Table 72. Characteristics of interviewed patients compared to the rest of the study population

Parameter	Interviewed* (n = 48)	Not interviewed* (n = 88)	P
Age in years (mean \pm SD)	64.3 \pm 10.1	71.2 \pm 11.0	0.0007
<i>Gender</i>			
Male	21 (43.8%)	48 (54.5%)	0.23
Female	27 (56.3%)	40 (45.5%)	
<i>Pharmacy region</i>			
Metro	25 (52.1%)	69 (78.4%)	0.002
Rural	23 (47.9%)	19 (21.6%)	
<i>RM status</i>			
RM-experienced	22 (45.8%)	28 (31.8%)	0.11
RM-naïve	26 (54.2%)	60 (68.2%)	
<i>Medication dispensed for co-morbidities[†]</i>			
Yes	42 (87.5%)	75 (85.2%)	0.71
No	6 (12.5%)	13 (14.8%)	
<i>Antidepressant dispensed[†]</i>			
Yes	9 (18.8%)	26 (29.5%)	0.17
No	39 (81.3%)	62 (70.5%)	
<i>Prescriptions dispensed at concession rate[†]</i>			
Yes	43 (89.6%)	81 (92.0%)	0.63
No	5 (10.4%)	7 (8.0%)	
Smoking history (pack years)	32.8 \pm 27.1	34.3 \pm 25.2	0.50
SGRQ score: symptoms	62.8 \pm 20.7	62.0 \pm 22.9	0.92
SGRQ score: activity limitation	61.8 \pm 27.2	65.1 \pm 26.8	0.39
SGRQ score: impact	35.9 \pm 21.5	37.8 \pm 21.2	0.74
SGRQ score: overall	48.1 \pm 21.1	50.6 \pm 20.9	0.44
HADS score: anxiety	7.0 \pm 5.0	7.1 \pm 4.6	0.86
HADS score: depression	5.9 \pm 3.7	6.0 \pm 3.8	0.95

*Figures represent mean \pm SD or number (%) of patients interviewed or not interviewed. [†]In the 12 months preceding identification.

When asked to describe their respiratory condition, patients used a variety of terms, including COPD, emphysema, asthma, chronic bronchitis, chronic cough and smoker's cough. A number were told they had a combination of conditions. Figure 41 displays the proportion of terms used to describe the condition.

Figure 41. Terms used to describe respiratory condition


5.3.3.2 Common themes relating to persistence

The common themes relating to persistence and non-persistence are summarised in Table 73.

Table 73. Common themes relating to tiotropium persistence

Drivers of persistence		Barriers of persistence	
Fear	Increasing importance	Lack of explanation and emphasis by GPs	
Faith in GPs		No perceived benefit	
Noticeable benefits		Side effects	
Desire to live longer with an improved quality of life		Confusion and fear of overmedicating	

5.3.3.3 Drivers of persistence

Fear of what might happen if tiotropium was not taken appeared to be the strongest driver for persistence. This was most commonly cited as fear of not being able to breathe or dying:

“I’m frightened that if I don’t take it [tiotropium], I’d wake up the next day not being able to breathe... I don’t want to die...”
(Female, 67)

“... I am too frightened to miss [a dose of tiotropium] in case I get an attack and can’t breathe. I don’t want to go down that track again, that choking feeling in my neck is terrible...”
(Female, 65)

Patients were also afraid of becoming dependent on oxygen therapy, requiring systemic corticosteroids, and being embarrassed in public by attacks of productive coughing. They believed that taking their tiotropium every day would prevent or delay these occurrences:

“The last thing I want to do is carry around a bottle with gas, it’s the last thing I want to do... I really don’t know what it would entail but the longer I can stay away from it the better.”
(Male, 63)

“Every time I tried to cut it [tiotropium] back I ended up in grief and I had the prednisolone for much longer than I would have liked so now I take the Spiriva[®] every day!” (Female, 44)

Fear was always greater amongst those who had known someone who had died with emphysema:

“I know of one bloke who’d still be here if he kept taking his medication. But he decided to give it all away. He died remarkably quickly.” (Female, 79)

“The last time I was in hospital I was in a ward with three other gentlemen and two of them died, through emphysema and the other had emphysema and cancer. So that has played a big part emotionally on my life. I still remember those people gasping for air and trying to breathe and the doctors telling them there was no more hope and just keep them comfortable... it’s distressing in the sense... when you see people gasping for air and all of a sudden they’ve stopped and they’re gone, there’s no coming back, they’ve gone.” (Male, 62)

Persistent patients also had a basic faith and trust in GPs to persist with their tiotropium, even if they were not sure how beneficial it was:

“There’s no point in seeking advice and then not taking it... He [the GP] said, ‘Take it! Take it!’ So I did feel once I’d taken it [tiotropium], that things were going better. It might have been pure coincidence.” (Female, 79)

“The doctors are trained, not me. If you are not going to take the tablets or do what they tell you, what is the point of going there in the first place?” (Male, 52)

“I would take it if he told me to take it. Why not? I can’t argue the point with him... they [doctors] tell you to do something, you do it don’t you?” (Male, 79)

Many persistent patients had experienced noticeable benefits from tiotropium:

“I was relieved to be put on it [tiotropium]. I can walk fast again and I go to the gym! I never want to be without it. I don’t want to get the same problems back that I had before. I like to feel better!” (Male, 71)

“... I find that’s [tiotropium] helped me a lot actually so I just keep on with it... It helped a lot. See I was using a puffer quite often but a puffer now will last me probably 3 weeks where before it was lasting me a week.” (Female, 61)

“You can’t cut off what helps you.” (Male, 58)

There was also a strong desire to live for longer with an improved quality of life amongst persistent patients:

“I want to see my granddaughter turn twenty-one. I want to see her turn ten, I want to see her turn five... We want to go to Hong Kong... Things like that you want to do and you want to do it full on.” (Male, 64)

“I don’t want to die! I’m having too much fun! Life is what you make it. I believe you gotta [sic] have plenty of friends and get out every day and I’m out every day and that’s the way I like it...” (Female, 65)

“I can work. Not really heavy, but work good. Before I was more or less lying down and relaxing.” (Male, 68)

Patients were often driven to persist with tiotropium for a variety of reasons, and the key drivers were often inter-related:

“It [tiotropium] was just one of the medications he [the GP] prescribed. He knows about it. I don’t... He’s the expert; I take his word for it [*TRUST IN GP*]... I started them [tiotropium], say, hypothetically on a Monday. By the next Monday I’d sent him [the doctor] a thank you card. I wasn’t sitting up in bed half the night, cough, cough, cough. I could breathe so much better [*NOTICEABLE BENEFITS*]... It’s keeping me comfortable. Quality of life I think is extremely important and my quality of life has been well maintained by the medication I take at the moment... I still can’t walk up hill but I am able to do household duties so much better. It’s such a relief [*DESIRE TO LIVE AN IMPROVED QUALITY OF LIFE*].” (Female, 71)

2.3.3.3 Non-persistence

The strongest barrier to persistence appeared to be a lack of explanation and emphasis by GPs as to why tiotropium had been prescribed:

“...He [the GP] said I had to take this inhaler [tiotropium] once a day for the rest of my life... He didn’t explain it or tell me what was wrong or why... If there was a problem I would’ve expected it [referral to specialist]. There obviously wasn’t a problem...” (Male, 63)

“With taking both of them [tiotropium and fluticasone combined with salmeterol], [GP’s name] said we’ll just try this Spiriva® ...

The Spiriva[®] was an afterthought in my mind. Because [GP's name] said lets try it, it's not quite the same importance as taking the Seretide[®]." (Female, 71)

"I get a bit breathless but the doctor has never said anything... They [his GPs] have never said anything about specific problems." (Male, 63)

This often led to a poor understanding of the diagnosed condition and unrealistic expectations of treatment, with patients discontinuing tiotropium if they did not perceive any benefit:

"I expected that my lung capacity would increase. I thought that's a good thing. It's [tiotropium] obviously going to loosen all the nicotine and tar up in my lungs. And I'm going to cough it up. So I expected to cough. I didn't cough. So I thought it's funny. I thought it's not doing its job. It's not worth having." (Male, 63)

"I tried it [tiotropium] and for about six weeks and I didn't see any benefit. I didn't notice anything... I'm not going to put anything into my body that I don't need to..." (Male, 51)

"Well with that Spiriva[®] I thought I'd feel it straight away but I didn't... So I was like given a script for this and I'm going to the chemist and I get it filled and then he shows me how to do it all and oh, it's a miracle you know. This miracle thing's going to fix me. I was a bit disappointed because it didn't." (Female, 50)

Unrealistic expectations of treatment also led to patients deciding to discontinue tiotropium on their own accord, if they who experienced side effects:

"All it did was give me an unproductive cough so if it couldn't help with me sputum there was no point in continuing." (Male, 75)

"I couldn't get on with that Spiriva[®], which I've got to go and tell him [the GP]... I was so hoarse I lost my voice and I

persisted with it for months and I couldn't clear my throat... I gave it some time, several months. I don't discard things quickly but I guess I wasn't prepared to put up with the side effects... (Female, 71)

Other patients were confused about the advice they had from GPs and were afraid of over-medicating, if they were already using another inhaled respiratory medication:

"He [the GP] said he didn't want to interfere with my other medication but I should give this a try. You know I didn't want to double up, they did the same thing or so I thought... I didn't see the point of taking both." (Female, 71)

"He [the GP] said I could take both, but I was a bit confused, they told me that the Spiriva[®] dilates the bronchial tubes just the same as the Seretide[®] only that the Spiriva[®] lasts longer and as it's only once a day... I'll switch over but I won't take both." (Female, 69)

5.4 Discussion

5.4.1 Recruitment of participants

5.4.1.1 Pharmacist participation

Approximately 50% of Tasmanian pharmacies use the Fred dispensing system. The responses of pharmacists to the expression of interest form showed a very high proportion of pharmacists (approximately 84%) used the Fred dispensing system and were willing to participate. However, it should be noted that the researchers targeted those pharmacists for recruitment who were known (or suspected) users of the Fred dispensing system, and who had successfully participated in data mining studies previously. The proportions of metropolitan and rural pharmacies (approximately 72% and 28% respectively) that participated in the study closely reflected the total proportions of metropolitan and rural pharmacies (80% and 20% respectively) in Tasmania.⁵⁹⁷

5.4.1.2 Identification of patients

An average of 36 patients were identified by each pharmacy. In-house testing of the MedeMine-for-COPD program and the identification criteria ensured an approximate even split of persistent and non-persistent patients per pharmacy; just over half of the identified patients were classed as persistent, and just under half were classed as non-persistent. The split of recent and late non-persistent patients was approximately even.

There was a significant difference in the proportion of persistent and non-persistent patients identified in rural and metropolitan pharmacies, with a greater proportion of persistent patients being identified in rural pharmacies. Anecdotal evidence suggests that pharmacists in rural pharmacies tend to have more time available to spend with patients and may be more likely to prompt patients to refill their tiotropium prescriptions. However, this difference may have simply been a result of patients tending to be more loyal clients in rural pharmacies. Indeed, once patients who were not regular clients had been excluded from each pharmacy, no significant differences between the persistent and non-persistent patients were observed in terms of pharmacy region.

5.4.1.3 Patient exclusions

MedeMine-for-COPD was programmed to include a maximum of 10 persistent patients per pharmacy. Upon running the MedeMine-for-COPD program, persistent patients were ranked by the date of first tiotropium dispensing, and after the 10 most recent dates, the rest of the patients were automatically excluded. Furthermore, an additional 11 pharmacies were recruited to the study in an attempt to increase the numbers of non-persistent patients. All of the persistent patients were excluded in these pharmacies under the reason 'not required.' This algorithm accounted for over half of all the patient exclusions.

The possibility of patients receiving tiotropium from other pharmacies was recognised as a potential limitation of the identification algorithm for non-persistence. It was possible that patients identified by the MedeMine-for-COPD program as non-persistent had simply received their tiotropium from a different pharmacy. Indeed, the most common reason for exclusion by the pharmacist was 'not a regular patient,' accounting for about three-quarters of all the exclusions made by pharmacists and nearly 90% of the non-persistent patient exclusions made by pharmacists.

In addition to the pre-defined exclusion criteria, three other reasons for exclusion emerged. These were 'patient has a language barrier,' 'patient is disabled' and 'patient is illiterate.' These were obvious barriers to completing a questionnaire and/or an interview.

It was not surprising that no persistent patients were excluded as being deceased, as the identification algorithm specified that persistent patients had to have received tiotropium recently (at least two supplies in the last 90 days). In addition, no persistent patients were excluded for being younger than 40 years old. It was probably less likely that patients under the age of 40 were diagnosed with COPD, and were probably more likely to have been prescribed a short trial of tiotropium for another condition, such as asthma.

5.4.1.4 Patient participation

It was not surprising that significantly more persistent patients agreed to participate than non-persistent patients. It is plausible that non-persistent patients did not believe the study would be relevant to them and therefore did not participate. This was despite the fact that the patient information sheet (Appendix 47) stated that the researchers were interested in studying people's experience with respiratory medication regardless of whether they had ceased their medication.

It is essential that the offer of incentives be kept in mind when interpreting patient response rates in this study. It was interesting that signing a consent form seemed to have more of an effect on response rates than the offer of monetary incentives. After sending out invitations to participate with the offer of incentives, approximately one-third of the patients consented to participate. This initial response rate of approximately 30% was considered to be quite low, given that the average patient response rate to postal questionnaires (with monetary incentives) reported in medical journals is approximately 50-80%.⁵⁹⁸⁻⁶⁰⁰ The low response rate for patients consenting to participate may have led to a degree of self-selection bias, which should be borne in mind when interpreting the results. However, after signing the consent form, the responses to the questionnaire rose to over 90%.

5.4.2 Quantitative analyses

5.4.2.1 Consenting patients' demographics and dispensing data

The finding that significantly more non-persistent patients were RM-naïve was in keeping with the results of a Canadian study of treatment persistence in COPD.⁵⁶⁵ Cramer *et al.* reported that most RM-naïve patients had significantly shorter treatment persistence for tiotropium than RM-experienced patients (27% versus 55% at 12 months, respectively, $P < 0.0001$). The authors explained this finding based on the assumption that previous use of respiratory medications may be a marker for respiratory disease severity and therefore an increased likelihood of medication persistence.

It was not surprising that patients who were dispensed medications for co-morbidities in the past 12 months were significantly more likely to be persistent with tiotropium. The collection of other medications would bring the patient into more regular contact with their community pharmacist, who could have monitored the patient's supply of tiotropium, and reminded them to collect their next supply and when they were due for a new prescription.

The likelihood of persistence was not statistically different between patients who had and had not received antidepressant medication in the past 12 months. This was a reasonable finding, given the multitude of indications for antidepressant medication, which is not always used to treat depression, and may have been used to treat other conditions such as neuropathic pain, anxiety and urge incontinence. Furthermore, patients who were non-persistent with tiotropium may have also been non-persistent with antidepressant medication. Therefore, patients' HADS scores were probably a more reliable test of whether mental state had any effect on persistence, as discussed later.

In the Australian population, use of respiratory medications is reported to be higher amongst people living in metropolitan areas, who may have more accessible healthcare services, and people with concession cards, who are able to purchase medications at a much cheaper price.²⁷⁰ It was therefore expected that tiotropium persistence would be higher amongst metropolitan and concessional patients. However, the low number of rural patients and non-concessional patients may have prevented any statistically significant difference in persistence from being detected. It was reasonable that more

than 90% of all patients were concessional, given that the average age was over 60 years; thus many patients would have been pensioner-concession cardholders.

5.4.2.2 Exposure to COPD risk factors

No significant differences between the persistent and non-persistent patients were observed in terms of previous work exposure to dust, gas or chemical fumes, current exposure to passive cigarette smoke at home, current smoking status, number of cigarettes smoked per day or pack years. Exposure to these risk factors can be divided into current exposure (current exposure to passive cigarette smoke at home, current smoking status and number of cigarettes smoked per day) and previous exposure (previous work exposure to dust, gas or chemical fumes, ever regularly smoked cigarettes and pack years). It is understandable that previous exposure may not affect current behaviours in persistence. While it is conceivable that current exposure to COPD risk factors (particularly self-inflicted exposure) may predict persistence to COPD medication, the low numbers of patients who were currently exposed to risk factors may have prevented any statistically significant difference in persistence from being detected.

5.4.2.3 Respiratory-specific health status

Although there were no statistically significant differences between the persistent and non-persistent patients' SGRQ scores, dissimilarities between the Impacts score for persistent and non-persistent patients exceeded the threshold for a clinically significant difference of four units.⁵⁹³ The minimum clinically important difference is the threshold that detects a 'just-noticeable-difference' within or between patients.⁶⁰¹ Taking the minimum threshold for a clinically important difference into account, non-persistent patients displayed a higher degree of impairment. In particular, the Impacts component of the SGRQ was made up of questions that assessed the impact of COPD on daily life, activities and work, as well as the impact of respiratory medication on daily living. A possible explanation is that persistent patients were benefiting from the effects of appropriate drug treatment, and therefore displayed fewer disturbances of psychosocial function due to COPD.

5.4.2.4 Illness perception

Persistent patients had higher scores for how much control they felt they had over their respiratory condition, and for how much they thought their treatment could help their respiratory condition. It is likely that perception of treatment control and personal control are inter-connected. To speculate, a patient who believed their treatment could not help their condition may have felt that they did not have any control over their condition as a consequence. It is therefore reasonable to expect that if a patient believed that tiotropium did not and could not help their respiratory condition, they may have chosen to cease their therapy. This finding is consistent with the Health Belief Model,^{602,603} which suggests that a patient's perception of the effectiveness of a recommended action (e.g. taking medication) predicts the likelihood of taking that action. This is also consistent with the qualitative analysis, with many non-persistent patients describing a lack of perceived benefit from treatment with tiotropium.

Available data suggests that a stronger emotional representation of illness, that is, how much an illness affects a person emotionally, has been negatively associated with personal control and treatment control beliefs, and a stronger belief in treatment control has been associated with fewer symptoms associated with the illness.⁶⁰⁴ In addition, people who have not yet received a diagnosis for their symptoms report lower treatment control beliefs.⁵⁸¹ This is also in keeping with the qualitative analysis of non-persistent patients, with many patients describing a lack of explanation and emphasis by GPs as to why tiotropium had been prescribed, leading to a poor understanding of the diagnosed condition and unrealistic expectations of treatment.

5.4.2.5 Beliefs about medicines

A number of studies have reported that medication beliefs explain a significant portion of variation in medication non-adherence.^{266,605-607} This study demonstrated that non-persistent patients were significantly more likely to believe that medicines do more harm than good. This is consistent with reports that patients' fear of adverse effects is an important barrier to medication adherence.⁶⁰⁸⁻⁶¹¹ This finding is also consistent with the Health Belief Model,^{602,603} which suggests that a patient's perception of susceptibility (e.g. risk of suffering an adverse drug event), severity (e.g. seriousness of an adverse drug event), barriers (e.g. tangible and psychological costs of taking the prescribed medication) and benefits (e.g. positive consequences of taking the prescribed

medication) predict behavioural response to treatment. It is evident that increased awareness of patients' beliefs about medicines is needed among healthcare providers, and patients should be encouraged to express their views about medicine in order to optimise and personalise their therapy.

Low agreement with the statement "medicines do more harm than good" remained a significant independent predictor of persistence in the multivariate analysis. This study therefore identified a specific patient cognition relating to medication that can act as either a help or a hindrance to treatment persistence. Identification of this cognition can facilitate the development of interventions that modify or take account of specific patient perceptions.

5.4.2.6 Medication adherence behaviour

Non-persistence represents a form of non-adherence. It was therefore not surprising that persistent and non-persistent patients had significantly different scores for more than half of the TABS items, or that the total adherence and non-adherence scores remained significantly different. Non-persistent patients had significantly higher scores than persistent patients on three of the non-adherence items ("I get confused about my respiratory medications," "I vary my recommended management depending on how I am feeling" and "I put up with my respiratory problems before taking any action"). Interestingly, two of these items ("I get confused about my respiratory medications" and "I vary my recommended management depending on how I am feeling") were found to be significant independent predictors of non-adherence in an Australian study of patients with COPD.⁵⁷²

Persistent patients had significantly higher scores than non-persistent patients on two of the adherence items ("I have strict routines for using my regular respiratory medications" and "I keep my respiratory medications close to where I need to use them"). Out of all the TABS items, the item "I have strict routines for using my regular respiratory medications" had the strongest significant difference between persistent and non-persistent patients ($P < 0.001$), and remained a significant independent predictor of persistence in the multivariate analysis. Qualitative analysis provided further insight to why persistent patients had strict medication routines, and persisted with the medication.

5.4.2.7 Anxiety and depression

This study showed no significant differences in persistent and non-persistent patients' scores for the Hospital Anxiety and Depression Scale. This is consistent with the finding that the likelihood of persistence was not statistically different between patients who had and had not received antidepressant medication in the past 12 months.

Psychiatric co-morbidity is common in patients with COPD. Up to 40% are clinically depressed; a similar number also experience moderate to high levels of anxiety.⁶¹²⁻⁶¹⁶ Both depression and anxiety result in lower health status and greater functional impairments, and depression has been linked with lower medication adherence.⁶¹⁷ Additionally, a stable family life with caregivers who provide support and encouragement is associated with improved medication-taking behaviour.⁶¹⁸

The instruction at the introduction to the HADS is to best indicate how the respondent has felt 'in the past week.' As it is a measure of current symptoms of mood disorders, this may have limited the likelihood of the scores relating to persistence, because the decision to cease therapy may have occurred up to 12 months ago according to the definition of non-persistence.

5.4.2.8 Multivariate analysis

Low agreement with the statement "medicines do more harm than good" and high agreement with the statement "I have strict routines for using my respiratory medications" were found to be significant independent predictors for persistence. Furthermore, a significant negative correlation was demonstrated between the two items; patients who agreed that medicines do more harm than good were less likely to have strict routines for using their respiratory medications. As the former item is a belief, whereas the latter item is a behaviour, it is reasonable to expect that patients' perception of the risks and benefits of medication determine their routinisation of respiratory medication use. This relationship seems to support the possibility that patients' perception of the risks and benefits of medication could be independently targeted for an interventional strategy to improve persistence and medication-taking behaviour.

5.4.3 Qualitative analysis

5.4.3.1 Characteristics of interviewed patients

The interviewed patients' characteristics were not exactly matched to the rest of the consenting patients. This can be explained by the fact that the interviewed patients were a convenience sample rather than a random sample and the fact that representation in the sample was largely due to the willingness of participants or whether they had time to participate in an interview. Other drivers for the difference included cost and scheduling of interviews (scheduling being more important) in that the interviews had to be done in specific geographic locations.

Interviewed patients were significantly younger than the rest of the consenting patients. This was not surprising, as the younger patients tended to be more desirable candidates for interviewing, in that they tended to have more detailed memories of the initial diagnosis of their respiratory condition and initial prescription of tiotropium. Furthermore, only one patient over the age of 80 was interviewed, as the other two patients over the age of 80 who had booked in for an interview were too ill to participate.

A significantly greater proportion of interviewed patients were identified in rural pharmacies compared to the rest of the consenting patients. Of the patients who were not interviewed, less than a quarter were identified in rural pharmacies, whereas an approximately even number of metropolitan and rural patients were asked to participate in interviews to ensure any drivers and barriers relating to region could be identified. Interviewed patients were representative of the rest of the consenting patients in terms of gender, whether medications had been dispensed for co-morbidities, whether antidepressants had been dispensed or whether prescriptions had been dispensed at the concessional rate in the past year.

5.4.3.2 Persistence

Fear of what might happen if tiotropium was not taken appeared to be the strongest driver for persistence. The consequences of not taking tiotropium that patients were fearful of were both short-term (not being able to breathe, embarrassment due to coughing and producing phlegm in public and requiring systemic corticosteroids) and long-term (missing out on life and requiring supplemental oxygen therapy). Other

research has demonstrated that patients with COPD who are adherent with their medication have a higher perceived influence of management over the future course of COPD.⁶¹⁹

Persistent patients also demonstrated a basic faith and trust in their GP's advice. This trust was apparent for both long-term GPs (10-15 years) and where patients had new doctors every two to three years. Some younger patients, while they respected their doctor's training, did not endow all GPs with the same level of confidence and respect, as did the older patients. In most cases, patients felt that their tiotropium did make 'some' difference but their trust in their GP leant itself towards ensuring that they trialled their medication for long enough for it to take effect. However, those with considerable faith in their GP accepted their explanations more fully and sometimes took treatment solely on the GP's advice. Satisfaction and faith in the treating doctor are known from other studies to be critical for optimal adherence in both COPD and other patient populations.^{572,620}

Not surprisingly, persistent patients had experienced noticeable benefits from tiotropium. Persistent patients' expectations of the benefits of tiotropium seemed to be more realistic than those of the non-persistent patients. For example, persistent patients expected tiotropium to ease their shortness of breath, whereas many non-persistent patients expected a reduction of phlegm production and coughing. An Australian study demonstrated that patients with COPD who are adherent with their medication have greater confidence that their management will keep their illness under control.⁵⁷²

Persistent patients possessed a strong desire to live for longer with an improved quality of life, and believed that continuing to take their tiotropium everyday would help them achieve these things. These patients focussed more on the long-term benefits of taking tiotropium rather than day-to-day improvements, usually had a positive outlook on life and had a supportive family.

5.4.3.3 Non-persistence

The strongest barrier to persistence appeared to be a lack of explanation and emphasis by GPs as to why tiotropium had been prescribed, leading to a poor understanding of the diagnosed condition and unrealistic expectations of treatment. It is known that poorer

patient knowledge about their disease and treatment negatively affects medication-taking behaviour.^{572,620}

Interestingly, a recent qualitative study of Tasmanian GPs found that making a diagnosis of COPD by GPs is often delayed, and that this delay may be intentional.⁶²¹ The study also found that even after a diagnosis had been made, it was often not communicated to patients. Not communicating a formal diagnosis to patients was rationalised by misperception of patients' unwillingness to be given a diagnosis and GPs' pessimistic attitudes to prognosis.⁶²¹ These results highlight the need for efforts to increase the awareness and understanding of COPD in the community, and education for GPs to reduce their nihilistic attitudes towards the condition.

While a lack of explanation and emphasis by GPs as to why tiotropium had been prescribed was identified as a barrier to persistence, it was not a sole reason for discontinuation of therapy. Rather, it was likely to lead to unrealistic expectations of treatment and misconceptions about the risks and benefits of tiotropium. These patients were then more likely to discontinue therapy for the common reasons identified; a perceived lack of benefit, experiencing adverse effects, fear of potential adverse effects and confusion with fear of over-medicating. Beliefs about medication not working and concerns about long-term effects have previously been identified as reasons for non-adherence amongst patients with COPD.⁶¹⁹ The reasons for non-persistence with tiotropium are consistent with the Health Belief Model,^{602,603} and the results demonstrate that patients tend to perform their own-risk/benefit analysis on the prescribed medication, the outcome of such an analysis being strongly influenced by the emphasis given by GPs at the time of initial prescribing.

5.4.4 Study limitations

There are limitations to this study, which are integral to the interpretation of both the quantitative and qualitative findings. An important limitation was the presumption that patients collected their medication exclusively from the pharmacy from which they were identified. This may have resulted in incorrect classification of patients as non-persistent, if they collected tiotropium from another pharmacy. To account for this, patients who more obviously used multiple pharmacies were excluded at the outset, however this may have resulted in the exclusion of some patients who may have been

more likely to be non-persistent or non-adherent because they did not have a consistent relationship with their pharmacist.

It is also important to recognise that dispensing data does not verify administration. The data does, however, directly address the question of availability. Clearly, patients cannot persist with a drug therapy if they have not obtained the prescribed drug, so persistence is secondary to availability.

While this study used quantitative and qualitative methods to analyse medication persistence, it did not provide any evidence as to which measure has more accuracy in predicting persistence. Medication persistence and adherence can be estimated using a variety of methods, including the use of biologic assays of drug in body fluids, pill counts, electronic monitoring and self-report, and it is recognised that each method has its limitations and that a gold standard measure does not exist.⁵⁵²

Lastly, there may have been a degree of self-selection bias, as significantly more persistent patients agreed to participate than non-persistent patients. It is therefore possible that more predictors for non-persistence that were not identified in this study may exist. This was controlled for in some degree by the dispensing data comparison of consenting and non-consenting patients, which revealed no significant differences. The low response rate for patients consenting to participate (approximately 30%) may have also led to a degree of self-selection bias, which should be borne in mind when interpreting the results.

5.5 Conclusions

This was an innovative study, which utilised a largely untapped health resource - community pharmacists and their computerised prescription data - to help identify patients with COPD as evidenced by their use of tiotropium. The data mining software, compatible with the Fred dispensing system, identified an average of 15 non-persistent patients per pharmacy. Approximately 2,250 of the 4,500 pharmacies in Australia use Fred Dispense. Therefore, if the software was available to all compatible pharmacies in Australia, approximately 33,750 non-persistent patients could be identified and targeted for an intervention aiming to improve tiotropium persistence.

The quantitative and qualitative analyses of patients who were identified by their pharmacy dispensing records as persistent or non-persistent with tiotropium identified

key variables relating to medication persistence. In the quantitative analysis, low agreement with the statement “medicines do more harm than good” and high agreement with the statement “I have strict routines for using my respiratory medications” were found to be significant independent predictors for persistence. In the qualitative analysis, patients’ perceptions of the risks and benefits of tiotropium, which appeared to be strongly influenced by personal experience and the prescriber’s attitude, were found to be determinants of persistence. The drivers of persistence identified in this study were consistent with perceptions that taking tiotropium was more likely to result in favourable outcomes, whereas the barriers of persistence were consistent with perceptions that taking tiotropium was more likely to result in ineffectual or harmful outcomes. Identification of these variables can facilitate the development of interventions that modify or take account of specific patient adherence behaviours and perceptions about the risks and benefits of medication. It is evident that increased awareness of the patients’ beliefs about medicines is needed among healthcare providers, and patients should be encouraged to express their views about medicine. In particular, patients need to be more informed about the long-term benefits of tiotropium therapy and that, in most cases, the potential benefits outweighs the potential risks of therapy. The development of a more collaborative relationship between patients and healthcare providers is also necessary in order to optimise and personalise their therapy and prompt patients to refill their tiotropium prescriptions.

PART FOUR:

GENERAL DISCUSSION AND CONCLUSIONS

All of the work described in this thesis showed that community pharmacists and their dispensing records can be effectively utilised to identify management issues in patients with asthma and COPD. The use of electronic information technologies to manage health information is likely to generate many benefits for patients in terms of improved quality and continuity of care. However, it also greatly increases the potential for patient information to be collated, to be combined with information from different sources, and to be used and disclosed - all potentially without the knowledge of the patient, for purposes that they may or may not consider to be in their interests.⁶²²

Throughout the studies performed in this thesis, there were two potential points in the utilisation of health information that may have raised privacy concerns amongst patients:

- The use of data mining by the community pharmacist to identify and contact patients; and
- The analysis of de-identified dispensing records by the researchers.

Although protecting confidentiality in healthcare is usually paramount, the legal obligation is not absolute. There are some occasions when sharing information is encouraged. In the case of community pharmacists using dispensing records to identify and contact patients with asthma or COPD management issues, they are acting in the best interests of the patient's health. In accordance with the National Privacy Principles, health information may be used or disclosed for a secondary purpose other than the primary purpose for which it was collected if the use by a healthcare professional is reasonably necessary for provision of a further health service to the patient.⁶²³

- An Australian qualitative study found that while patients see their personal health information as private, they want to share this information with healthcare professionals in order to facilitate communication and good treatment decisions

In fact, in contrast to family, friendship circles and community contexts, the patient-healthcare professional relationship was the only one where there was no reservation about sharing the health information.⁶²⁴ Another Australian study recently found that

older patients with multiple chronic medical conditions believe that improving the quality of their healthcare outweighs the risk of losing health information privacy.⁶²⁵

The analysis of patients' de-identified dispensing data without obtaining consent in this study brings up a second issue relating to patient privacy. There is professional consensus that consent must be obtained from patients prior to their inclusion in research studies, but there is less agreement when such involvement is restricted to collecting information from patient records. Although some believe that failure to seek consent is always wrong,⁶²⁶ it has been argued that collection of data from records without seeking patient consent can be justified, providing certain minimal conditions are met.^{627,628} These conditions include research when the patients' data is de-identified, the invasiveness and risks of the research are negligible, the requirement for informed consent might jeopardise methodological rigour, and a research ethics committee has waived the requirement to seek consent for pressing and justifiable reasons.

There is growing concern that sharing health information data, in particular for research, may influence patients' willingness to divulge clinically relevant information to healthcare professionals. This in turn may compromise professionals' ability to provide optimum care. It is important that patients trust healthcare professionals and are not deterred from seeking treatment for fear that their personal information may be disclosed without authorisation or consent.⁶²⁹

A study carried out in the United Kingdom aimed to explore the views and attitudes of patients regarding the sharing of health information data, with particular reference to data sharing for research purposes and the impact that this may have on the trust between patients and healthcare professionals.⁶³⁰ Interestingly, patients generally saw concepts such as audit and national disease registries positively and were happy for anonymous data to be shared in order to monitor and promote good standards of care. Furthermore, surveys from 1,719 patients with asthma and 1,710 patients with stable angina showed that only 9.8% refused consent to the collection of data from their clinical records.⁶³¹

Although privacy must be safeguarded, the safeguards need not be inconsistent with the goal of obtaining complete data and advancement of knowledge. Sadly, around the world, data repositories are now at risk of significant bias because concern about patient privacy has led to the requirement that consent be obtained before an individual's data

can be included.⁶³² For example, a Canadian study showed that obtaining written informed consent for inclusion in a stroke registry led to important selection bias.⁶³³ Similarly, in the 2006-07 pilot asthma study, intervention patients who returned the baseline questionnaires were found to have a significantly higher preventer-to-reliever ratio and daily usage of ICS than those who did not return the questionnaires. In other words, patients who had better asthma management tended to return the questionnaires.^{5,304} Thus, patients who actively participate in research are often not representative of the entire population of interest, a phenomenon termed ‘authorisation bias.’⁶³⁴ These findings highlight the importance of developing new privacy legislation and policies allowing waivers of informed consent for minimal-risk research on the ground of impracticability. A reasonable alternative way of obtaining data from a representative sample of patients is to collect de-identified data from patient’s medical records without obtaining consent but with appropriate confidentiality safeguards in place.⁶³³ Indeed, this method was employed as a way of collecting and analysing medication data in all of the studies described in this thesis.

Issues in asthma and COPD management in Australia are well documented.^{3,4} Despite its national health priority status, the management of asthma remains a problem in Australia. Research has shown that a significant proportion of people with asthma still do not have a written AAP, have poorly controlled asthma and over-rely on their reliever medication.⁶ Patients need to be more educated about asthma and the need for regular preventive therapy and monitoring, so that their perceptions of asthma control are more realistic. Healthcare professionals should also work together to encourage patients to be more forthcoming about their asthma symptoms, so that their therapy can be tailored and optimised to ensure adequate asthma control.

There is irrefutable evidence that COPD is a significant public health problem in Australia. Unlike asthma, however, it is not a National Health Priority area, despite a mortality rate ten times that of asthma and annual costs that exceed \$8 billion.^{7,8} This suggests a lack of awareness of the present and future burden from COPD, perceptions and societal stigmas around its cause, and insufficient understanding of its public health importance.⁹ In order to reduce the burden of COPD in Australia, it is imperative that healthcare professionals develop a collaborative management approach to ensure the early and accurate diagnosis of COPD, which can then drive the implementation of effective treatments. Patients should also be encouraged to express their views about the

condition and its treatment in order to optimise and personalise their therapy, ensuring adherence and persistence with prescribed medications.

Pharmacists are ideally placed in the healthcare system to address asthma and COPD management issues and they have the necessary skills to communicate with other healthcare providers and patients themselves to improve these conditions. There is enormous scope for community pharmacists to become the feedback link between patients and GPs, which would answer the societal need for improved management of asthma and COPD. Community pharmacists are trained in counselling and educating patients about their condition and prescribed medications, and have access to patients' dispensing records, meaning they are uniquely placed to monitor medication adherence issues.

Community pharmacists assisted in the implementation of all of the projects described in this thesis. While there clearly is the potential for community pharmacists to have an impact in improving the management of asthma and COPD, such approaches are most likely to be successful if they can be easily integrated into pharmacists' workflow, and the need for further research testing strategies that are pragmatic in busy community pharmacies has been identified.¹⁰⁻¹⁴

Time has clearly been identified in previous studies as a major factor that significantly prevents community pharmacists from undertaking any additional extended role in healthcare.^{11-14,340,341} The workload in community pharmacy practice is such that research is perceived as having low priority because it would have to be taken on as an additional role.¹¹ The projects described in this thesis required minimal time and additional training on the part of the pharmacist, and could be easily integrated into their workflow. Pharmacists assessed the projects favourably, and believed that they were a positive move towards recognition of their role in patient care.

This body of work presents a number of solutions to issues surrounding the management of asthma and COPD in the community. With the knowledge gained from the results of these projects and using aspects of interventions described in this thesis, community pharmacists have the potential to dramatically improve the management of these conditions. Community pharmacists have the necessary skills to communicate with other healthcare providers and patients themselves to improve the management of asthma and COPD, and software tools such as MedeMine can aid in the efficient

targeting of patients. A national roll-out of the asthma intervention, and a specifically designed COPD intervention may result in better health outcomes for patients, and ultimately less burden on the health system.

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APPENDICES

Appendix 1. GP invitation letter



Improving the management of asthma

<Date>

Dear <GP's name>

The Tasmanian School of Pharmacy is currently undertaking a follow-up research project aiming to determine the feasibility of a community pharmacy intervention to improve the management of asthma, conducted in 2006-07.

As part of this follow-up project, general practitioners, community pharmacists and patients who were previously involved in the intervention project will be interviewed, to explore their views on the management of asthma, their perceived roles of health professionals and their perceived feasibility of a community pharmacist initiated intervention. This will help to determine what practice changes are required to successfully implement the asthma intervention on a national scale.

How can you help?

All you have to do is:

1. Read the enclosed Project Information Sheet and Participant Consent Form
2. Sign the Participant Consent Form and send it to the University using the postage paid envelope provided or fax it to 6226 7627.

Once your consent form is received, a researcher will contact you to schedule a face-to-face interview. We estimate that the interview will take 20 to 30 minutes, and upon the completion of the interview, you will receive remuneration of \$200 for your time.

If you have any queries regarding the project's procedures, please contact Bonnie Bereznicki at the Tasmanian School of Pharmacy on 6226 2191 or bonnie.bereznicki@utas.edu.au.

Yours sincerely,

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Appendix 2. Project information sheet



Improving the management of asthma

PROJECT INFORMATION SHEET

Why this research is needed

Asthma affects over 2 million Australians and causes thousands of hospital admissions each year. Recent findings suggest that the management of Asthma in Australia needs to be improved.

Aim of this research

The aim of this research is to gain insight into people's perceptions of community pharmacist initiated interventions to improve asthma management.

About the project

The project is being conducted by the Tasmanian School of Pharmacy and is a follow-up of a previous Tasmanian intervention project that encouraged people with poorly controlled asthma to review their condition with their doctor. The intervention resulted in a three-fold improvement in the management of asthma, measured by a significant shift towards patients using preventer medication and relying less on reliever medications. There were also significant improvements in self-reported asthma control and quality of life.

As part of this follow-up project, people with asthma, as well as doctors and pharmacists will be interviewed, exploring their views regarding the management of asthma and the feasibility of a community pharmacist initiated intervention. The project will form part of a PhD thesis, which aims to improve the management and quality of life of Tasmanians with asthma.

How can you help?

All you have to do is:

1. Read and sign the enclosed consent form
2. Send it to the University using the postage paid envelope or fax it to 6226 7627.

What happens next?

If you return a signed consent form, a researcher will contact you, and a time will be arranged for a face-to-face interview. An expert in qualitative research will conduct all of the interviews, and you will not be required to discuss any issues of a sensitive nature. With your permission, the interview will be digitally recorded, so that common views amongst interviewees can be compared. The interview will take no more than one hour, and upon the completion of the interview, you will receive remuneration of <amount> for your time.

Special note on privacy

Please be assured that your privacy will be maintained, and no one at the University will be able to identify the information that you provide. Your name and address will not be sent to the University unless you send them the signed consent form.

Appendix 3. Participant consent form



Improving the management of asthma

PARTICIPANT CONSENT FORM

By signing this consent form I am agreeing to participate in this research project and declare that;

- 1 I have read and understood the 'Project Information Sheet' for this research project.
- 2 I acknowledge that the nature, purpose and contemplated effects of the project so far as it affects me, and I understand that my consent is given voluntarily.
- 3 I understand that the project involves the following procedures:
 - Upon signing the consent form and mailing it to the researchers, I will be contacted regarding the scheduling of a face-to-face interview.
 - The interview will be about my views on asthma, its management, and the role and feasibility of a community pharmacist initiated intervention to improve the management of asthma in the community.
 - The interview will be digitally recorded and analysed.
- 4 I understand that all research data will be securely stored on the University of Tasmania premises for at least five years, and will then be destroyed.
- 5 Any questions that I have asked have been answered to my satisfaction.
- 6 I agree that research data gathered from me for the study may be published provided that I cannot be identified as a participant.
- 7 I understand that the researchers will maintain my identity confidential and that any information I supply to the researchers will be used only for the purposes of the research.
- 8 I agree to participate in this investigation and understand that I may withdraw at any time without any effect, and if I so wish, may request that any data I have supplied to date be withdrawn from the research.
- 9 I understand that I am not giving up my legal rights by signing this consent form.
- 10 I understand that the project has received ethical approval from the Tasmanian Social Sciences Human Research Ethics Committee. I have been provided with adequate contact details if I wish to express any concerns of an ethical nature or complaints about the manner in which the project is conducted.

Name of Participant:.....

Address:.....

.....

Daytime telephone number:..... Email address:.....

Preferred day and time of interview:.....

Signature of Participant: Date:.....

**Please mail the signed consent form to the University of Tasmania
in the postage paid envelope provided or fax it to 6226 7627.**

This project is funded by the Commonwealth Department of Health and Ageing and the Asthma Foundations Australia via an Asthma Targeted Intervention Grant.

Appendix 4. Pharmacist invitation letter



Improving the management of asthma

<Date>

Dear colleague,

The Tasmanian School of Pharmacy is currently undertaking a follow-up research project aiming to determine the feasibility of a community pharmacy intervention to improve the management of asthma, conducted in 2006-07. The intervention encouraged people with poorly controlled asthma to review their condition with their doctor. The result was a three-fold improvement in the management of asthma, measured by a significant shift towards patients using preventer medication and relying less on reliever medications.

As part of this follow-up project, community pharmacists, general practitioners and patients who were previously involved in the intervention project will be interviewed, to explore their views on the management of asthma, their perceived roles of health professionals and their perceived feasibility of a community pharmacist initiated intervention. This will help to determine what practice changes are required to successfully implement the asthma intervention on a national scale. The project will also form part of a PhD thesis, which aims to improve the management and quality of life of Tasmanians with asthma.

We are writing to you to ask for your involvement in this important project. Should you wish to assist us, you will be asked to participate in a face-to-face interview and/or assist with the recruitment of patients for interviews. An expert in qualitative research will conduct all of the interviews, and you will not be required to discuss any issues of a sensitive nature. We estimate that the interview will take 30 to 40 minutes, and upon the completion of the interview, you will receive remuneration of \$100 for your time.

We are also inviting pharmacists to assist with the recruitment of patients for face-to-face interviews. If you are interested in participating in the recruitment phase, you will be asked to mail invitation letters and consent forms to approximately 10 patients who previously participated in the intervention. A researcher will provide you with the ID numbers of former participants from your pharmacy. These codes are linked to the Fred dispensing system and will re-identify the patients, allowing you to send out invitation letters and consent forms. To protect patients' privacy, you will not be required to disclose any patients' identities to the researchers without their consent. We anticipate that this will require approximately 15 minutes of your time. In order to thank you for your assistance with the patient recruitment, we are offering \$50 to compensate you for your time. In addition, the project will cover associated stationery and postage costs.

The project has received ethical approval from the Tasmanian Social Sciences Human Research Ethics Committee. If you have any concerns of an ethical nature or complaints about the manner in which the project is conducted, you may contact the Executive Officer of the Tasmanian Human Research Ethics Committee (Tasmania) Network on 6226 7479 or human.ethics@utas.edu.au. You will need to quote ethics reference number H10378.

The project is being funded by the Asthma Foundations Australia, and it is intended that the results will be disseminated to Australian GPs and pharmacists by presentations at national meetings and in peer-reviewed journals. We can assure you that no identifying information relating to patients, doctors or pharmacists will be disseminated. All project results will be de-identified and pooled.

Enclosed is an "Expression of Interest" form for you to return to us. Please indicate whether or not you are willing and able to participate in a face-to-face interview and/or assist with the patient recruitment process. You can either fax the form it back to us on 6226 7627 or send it back to us in the reply paid envelope provided.

If you have any queries about this project please contact Bonnie Bereznicki at the Tasmanian School of Pharmacy on telephone 6226 2191 or email bonnie.bereznicki@utas.edu.au. We will be contacting you shortly to discuss your willingness to participate in this project.

Yours sincerely



Bonnie Bereznicki B.Pharm (Hons)
Clinical Research Pharmacist and PhD Candidate
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 26
Hobart Tasmania 7001
Ph (03) 6226 2191
Fax (03) 6226 7627
Bonnie.Bereznicki@utas.edu.au



Dr Shane Jackson B.Pharm (Hons) PhD
Senior Research Fellow
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania

Appendix 5. Pharmacist expression of interest form



Improving the management of asthma

Expression of Interest

Attention: Bonnie Bereznicki

- ☐ Yes, I am interested in participating in the research project, *Improving the management of asthma*, being conducted by the Tasmanian School of Pharmacy. In particular, I am interested in:
- ☐ Participating in a face-to-face interview, and/or
 - ☐ Assisting with the patient recruitment process
- ☐ Sorry, I am not able to participate in this project.

Name of Pharmacist(s) <pharmacist's name>

Pharmacy Name: <pharmacy name>

Pharmacy Address: <pharmacy address line 1>

<pharmacy address line 2>

Please return this form to the Tasmanian School of Pharmacy in the reply paid envelope provided or fax it to 6226 7627.

Private Bag 26 Hobart
Tasmania Australia 7001
Telephone 6226 2191
Facsimile 6226 7627
Bonnie.Bereznicki@utas.edu.au

Appendix 6. Pharmacist interview letter



Improving the management of asthma

Pharmacist interviews

<Date>

Dear <Pharmacist's name>,

Thankyou for expressing an interest in participating in a qualitative interview for the research project *Improving the management of asthma*, being conducted by the Tasmanian School of Pharmacy. Please find enclosed a Project Information Sheet and Participant Consent Form.

All you have to do is:

- 1. Read the enclosed Project Information Sheet and Participant Consent Form**
- 2. Sign the Participant Consent Form and send it to the University using the postage paid envelope provided or fax it to 6226 7627.**

Once your consent form is received, a researcher will contact you to schedule a face-to-face interview. We estimate that the interview will take 30 to 40 minutes, and upon the completion of the interview, you will receive remuneration of \$100 for your time.

If you have any queries or concerns about this project please contact Bonnie Bereznicki at the School of Pharmacy on telephone 6226 2191 or email bonnie.bereznicki@utas.edu.au.

Once again, thankyou for your assistance with our research.

Yours sincerely,

Bonnie Bereznicki B.Pharm (Hons)
Clinical Research Pharmacist and PhD Candidate
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 26
Hobart Tasmania 7001
Ph (03) 6226 2191
Fax (03) 6226 7627
Bonnie.Bereznicki@utas.edu.au

Dr Shane Jackson B.Pharm (Hons) PhD
Senior Research Fellow
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania

Appendix 7. Patient recruitment instructions



Improving the management of asthma

Patient recruitment instructions

<Date>

Dear <Pharmacist's name>,

Thankyou for agreeing to assist with the patient recruitment process for the research project *Improving the management of asthma*, being conducted by the Tasmanian School of Pharmacy. Please find enclosed <number> patient recruitment packs. Each pack contains a blank postage paid envelope, an Invitation Letter, a Project Information Sheet, a Participant Consent form and a University-addressed postage paid envelope.

The ID numbers of the former participants from your pharmacy are:

<ID number>

<ID number>

<ID number>

<ID number>

Entering these numbers, one at a time, into the patient field in Fred Dispense should identify the participants' names.

Once you have identified the potential participants, please write their name on the top of the Invitation Letter, and sign the letter. Please place the Invitation Letter, a Project Information Sheet, a Participant Consent Form and a University-addressed postage paid envelope inside a blank postage paid envelope and address the envelope to the patient, and place it in the mail.

Please note that no identifying information will be released to the researchers unless the patient signs the consent form and returns it to the University. Once your patients' consent forms are received, a researcher will contact them to schedule a face-to-face interview. We estimate that the interview will take no longer than one hour, and upon the completion of the interview, they will receive remuneration of \$50 for their time.

In order to thank you for your assistance with this study, we are offering \$50 to compensate you for your time and professional input. To receive payment, please generate a tax invoice for \$50 (inclusive of GST) with a description of *professional services rendered - ATIG project*, and mail or fax to:

Kimbra Fitzmaurice
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 26
Hobart TAS 7001
Facsimile: 6226 7627

Appendix 8. Patient invitation letter

<proprietor name>
<pharmacy name>
<pharmacy address line 1>
<pharmacy address line 2>
Ph: <ph num>

Improving the management of asthma

<Date>

Dear <patient's name>

The Tasmanian School of Pharmacy is currently undertaking a follow-up research project aiming to determine the feasibility of a community pharmacy intervention to improve the management of asthma, conducted in 2006-07.

As part of this follow-up project, people with asthma, as well as doctors and pharmacists will be interviewed, to explore their views on the management of asthma, their perceived roles of health professionals and their perceived feasibility of a community pharmacist initiated intervention. This will help to determine what practice changes are required to successfully implement the asthma intervention on a national scale.

How can you help?

All you have to do is:

1. Read the enclosed Project Information Sheet and Participant Consent Form
2. Sign the Participant Consent Form and send it to the University using the postage paid envelope provided or fax it to 6226 7627.

Once your consent form is received, a researcher will contact you to schedule a face-to-face interview. The interview will take no more than one hour, and upon the completion of the interview, you will receive remuneration of \$50 for your time.

Please be assured that your name and private information has not been released to the University. Your name and address will not be sent to the University unless you send them the signed consent form.

If you have any questions about this project, or your asthma, please give me a call at the pharmacy.

Yours sincerely,

<pharmacist's name>

Appendix 9. Discussion guide for qualitative interviews



Improving the management of asthma

DISCUSSION GUIDE

Background: Explain purpose of research: *To better understand the acceptance of professional activities by pharmacists directed at patients with asthma, in order to improve the national management of asthma.*

Note: This represents a guide rather than a set of specific questions. The purpose of the guide is to provide a framework for interviews, and to provide a list of the issues to be covered.

Briefly explain the following points:

- Research objectives:
 - Determine patient, pharmacist and GP perceptions regarding community pharmacist led interventions to improve asthma management.
 - Determine the barriers and enablers to the national implementation of a best-practice pharmacy led asthma intervention.
 - Determine what practice changes are required to successfully implement the asthma intervention on a national scale.
 - Confidentiality and anonymity, privacy
 - Timing: interview will take no longer than one hour patients, 30 mins GPs and 40 mins pharmacists
 - Honorarium: GPs: \$200, Pharmacists: \$100, Patients: \$50
-

1. Participant profile - Patient/community pharmacist/GP

The aim here is to get an overview of the respondent. Encourage respondents to describe themselves and situation, including:

- **Patients:** diagnosis, history of asthma (years),
 - Severity, e.g. any hospitalisations, difficulty in establishing drug regimen to control asthma
 - Use of asthma medications
 - List medications & dosage, regular vs non regular medications, OTC vs prescription

- Brief history of medications used
 - Age (estimated if necessary)
 - See a respiratory specialist and GP, other chronic conditions
 - NB: record gender & postcode

-
- **Community pharmacists:** years in community pharmacy practice (e.g. year of graduation), hours of community pharmacy practice per week, age, (NB record gender), remoteness (PhARIA) or postcode, owner or employee, accredited or not

-
- **GPs:** years in general practice (e.g. year of graduation and specialisation), hours of general practice per week, age, (NB record gender) number of patients in total practice, estimated percentage of patients with asthma in total practice, postcode
-

2. Perceptions of asthma management

Obtain a detailed picture of the respondent's thoughts on Australian asthma management. For patients/pharmacists this may be more prescriptive, but for GPs ask their strategy in managing patients with asthma, but in all prompt comment on:

- Their understanding of the effects of asthma on the Australian community (*GPs and pharmacists*)
- The need for improved asthma management in the community***** (*GPs and pharmacists*)
- The need of asthma prevention rather than treatment of symptoms (*all*)

Specifically **with patients** explore:

- Their knowledge of asthma, and perceived seriousness of the condition (is there a relationship between this and other chronic conditions? i.e. other chronic conditions may decrease perceived seriousness of patient's asthma)
- Their knowledge of asthma medication classifications and examples
 - Reliever/preventer
 - Long-acting/short-acting
- What they deem to be appropriate/adequate asthma management and how measured*****
- Risks/benefits of treating and not treating asthma (e.g. does the perceived risk of "steroids" outweigh the perceived risk of uncontrolled asthma?)

- Frequency of GP or specialist visits for asthma – probe on reason for visits (e.g. prescription requirement only, advice, asthma exacerbations, etc
- What they perceive the role of GPs and pharmacists to be in relation to asthma management (e.g. pharmacists as medication experts or as medication suppliers?)*****
- Who they go to for asthma management advice (e.g. specialists, GP, nurse, pharmacist, asthma educator, Asthma Foundation), also who of those individuals has helped them in the past. We could rank specialist, GP, nurses, pharmacist, asthma foundation, asthma educator in terms of:
 - Who is most accessible
 - Who is most approachable
 - Who is most threatening
 - Who is most trusted
 - Barriers/drivers (e.g. is their GP/pharmacist too busy?)

Specifically **with pharmacists**, explore their understanding of pharmacists' role in patient asthma management including:

- Supply of OTC and prescription medication
- Advice about asthma in general
- Counselling on asthma medication and inhaler technique
- Resources that are used
- What they think their primary role in relation to asthma management is*****
- Monitoring medication use – i.e. monitoring adherence to regular asthma medications and potential over-reliance on relievers
- Additional activities that they would like to be involved in, but for one reason or another can not or do not

Specifically **with General Practitioners**, explore:

- Which medications are most commonly prescribed by GP (preferences).
- Prescribing strategy with medications (which combinations, what doses)
- The development of patient Asthma Action Plans
- How patient symptoms are monitored by GP and instructions to patient re monitoring
- Overall management of asthma patients (suggested frequency of visits, patient self management, Asthma Action Plans)

- Perceived role of the community pharmacist in asthma management (e.g. pharmacists as medication experts or as medication suppliers?)*****

3. Discussion of community pharmacists led asthma intervention*****

Explain the first part of the ATIG study was to determine those patients who had potentially sub-optimally managed asthma.

The methodology used in the first study was:

- *The computer program examination of individual pharmacy records to identify patients with potentially suboptimal asthma management, as evidenced by the supply of three or more asthma reliever canisters in the past 6 months (which is equivalent to use of reliever medication three times per day)*
- *Postage of “intervention packs” to identified patients (by pharmacists)*
- *Intervention packs consisted of:*
 - *A personalised letter to the patient, alerting them to the fact that their use of reliever medication may indicate that their asthma is poorly controlled, and referring to their GP for a review of their asthma management;*
 - *A letter (with medication history) for the patient to hand to their GP*
 - *Educational material about asthma (from the Asthma Foundation)*
 - *Surveys for patients and GPs*

NB: The computer program created all personalised letters and surveys; all of the above was conducted by the community pharmacists, and the researchers did not have access to patients’ identities.

Specifically ascertain:

- **Patients** (exposed to the intervention): *NB: memory may be poor (first batch of letters sent Oct 2006, second batch sent April 2007; probing may be required)*

Ask patients to tell ‘their story’ of:

- *What their feelings were (or would be, if cannot remember) upon receiving an intervention pack in the mail*
- *How they felt (or would feel, if cannot remember), at the time of the intervention (an intrusion, welcomed etc)*
- *Recall (or would they, if cannot remember) of any action upon receiving an intervention pack (what action taken and why, and if not, why not?)*

- Reactions to pharmacists' involvement in this type of activity
 - Perceived barriers to taking action (ability to get an appointment with their GP, cost, perceived need for improved asthma control, etc)
 - Outcome, if any, of doctor visit
 - Adherence to the recommendations made at that time
 - Overall quality of asthma management
-

• **Pharmacists:**

Ascertain from pharmacists:

- The impact:
 - Patient identification had (or would have, if cannot remember) to their workflow
 - Of dispatch of asthma intervention packs
 - The positives and negatives of the intervention process
 - The relative efficacy of mailed versus face-to-face interventions (appropriateness/preference, likely uptake by pharmacists [time – barrier?])
 - Request suggestions on ways to improve the process
 - The viability of a national rollout of the program
 - Negative or positive feedback received
 - Patients
 - GPs/others
-

• **GPs:**

Ascertain from GPs:

- Impact (actual or perceived) of the intervention on the GP
 - Patients' likely adherence to suggested medication strategy resulting from the intervention
 - The value placed on the intervention process
 - The appropriateness of the intervention process
 - Suggestions for improvement or modification
 - The viability of a national rollout of the program
 - Positive or negative feedback
-

Thank the respondent for their time and pay incentive

Appendix 10. Pharmacist invitation letter



Improving the management of asthma

<Date>

Dear <Pharmacist's name>,

As a healthcare provider in your local community you would be aware that one of the major contributing factors to both morbidity and mortality of patients with asthma is their over-reliance of reliever medication, and under-use of preventive medication. A number of studies have shown that a high usage of relieve medication, relative to preventer medication, is associated with poorer clinical outcomes in asthma. With over 2 million Australians affected by asthma and with regular use of preventive medication estimated as low as 14%, we are seeking your assistance.

The Tasmanian School of Pharmacy at the University of Tasmania is currently undertaking a research project aiming to improve the management of asthma. We are writing to you to ask for your involvement in our project, which requires the use of Fred Dispense. A data mining software tool has been developed for Fred Dispense, which enables easy identification of patients who may benefit from review of their asthma therapy. Fred Dispense are aware and supportive of this project. Your role as the community pharmacist, if you choose to participate, will involve assisting with the patient identification process and the provision of an educational intervention, either by mail or in person over a six-week period.

The research project will assess the uptake and effect of face-to-face and mailed interventions, delivered by community pharmacists. Each participating pharmacy will be randomly assigned to deliver only one type of intervention. Use of the data mining software tool ensures that the intervention process is streamlined, and can be easily incorporated into busy community pharmacy practice. Please refer to the attached synopsis for details regarding the project's methods and procedures.

If you would like to be involved or require further information about the project, please complete the attached form and either fax it back to the Tasmanian School of Pharmacy on 6226 7627 or send it back to us in the reply paid envelope provided.

In order to thank you for your assistance with this study, we are offering \$200 to compensate you for your time and professional input into this project. In addition, the project will cover stationery and postage costs relevant to project participation.

The project has received ethical approval from the Tasmania Health and Medical Human Research Ethics Committee. If you have any concerns of an ethical nature or complaints about the manner in which the project is conducted, you may contact the Executive Officer of the Tasmanian Human Research Ethics Committee (Tasmania) Network on 62267479 or human.ethics@utas.edu.au. You will need to quote ethics reference number H9823.

The project is funded by the Department of Health and Ageing under the Fourth Community Pharmacy Agreement Research and Development Program, administered by the Pharmacy Guild of Australia. We can assure you that no identifying information relating to patients,

doctors or pharmacists will be disseminated. All project results will be de-identified and pooled for statistical analysis prior to a final report and publication.

If you have any queries regarding this project please contact Bonnie Bereznicki at the Tasmanian School of Pharmacy on 6226 2191. We will be contacting you shortly to discuss your willingness to participate in this project.

Yours sincerely,



Bonnie Bereznicki B.Pharm (Hons)
Clinical Research Pharmacist and PhD Candidate
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 83 Hobart
Tasmania 7001
Telephone 6226 2191
Facsimile 6226 7627
Bonnie.Bereznicki@utas.edu.au



Dr Shane Jackson B.Pharm (Hons) PhD
Senior Research Fellow
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania

Appendix 11. Project synopsis for pharmacists



Pharmacy dispensing records to identify and educate patients with suboptimal asthma management

Project Synopsis

This multi-centre project will develop strategic linkages across general practice and community pharmacy that, along with patient empowerment, will enhance the management of asthma. It will utilise a largely untapped health resource - community pharmacists and their computerised prescription data - to help identify and educate patients with suboptimal management of asthma. These patients will be identified from their dispensed medication history - in particular, a high provision of asthma reliever medication will be used. These patients will be provided with educational material from their pharmacist and advised to seek a review of their asthma management from their general practitioner.

A software application that extracts data from the market leading pharmacy dispensing software system in Australia (Fred Dispense) developed by the research team will be refined. Community pharmacies using the Fred dispensing system throughout Tasmania, Victoria and South Australia will be invited to participate, and with their permission, a researcher will install the software application on the dispensing computer.

The software will interrogate the dispensing history and produce a list of patients who have received six or more canisters of short-acting beta-2-agonists in the preceding 12 months (with at least three relievers in each six-month period). This indicates that the patient may be using on average three or more inhalations per day of reliever medication, which is in excess of contemporary guidelines for optimal asthma control. The software excludes patients receiving inhaled anticholinergic therapy or methylxanthines, indicating the likely presence of chronic obstructive pulmonary disease (COPD), or leukotriene-receptor antagonists indicating the probable diagnosis of severe asthma under the care of a respiratory specialist. Identified patients will be randomised to an intervention or control group. The participating pharmacist will examine the dispensing information for each patient identified and will be able to exclude patients from being sent an invitation to participate if they believe the patient is aged under 18 years, is residing in an aged care facility, is deceased, is significantly cognitively or would be alarmed excessively by participating in the project. Once a patient is deemed suitable for inclusion, the software will print materials required for an intervention pack.

This project will test the uptake and effectiveness of two types of community pharmacist interventions; intervention patients will either receive a mailed personalised letter and intervention pack or an 'alert flag' will be placed in their personal details within the dispensing system so that the pharmacist can give them an intervention pack with appropriate counselling on their next visit to the pharmacy. The intervention will occur over a six-week period, to allow time to mail intervention packs, or time for patients to visit the pharmacy to receive a face-to-face intervention. The intervention pack will consist of the following information:

- a computer-generated personalised letter, suggesting the patient visit their GP and seek a review of their asthma management.

- an educational leaflet about asthma,
- computer-generated asthma control, quality of life, and medication adherence questionnaires,
- a computer-generated letter (and medication history) to give to their GP, and
- a computer-generated GP satisfaction/perception survey of the intervention to give to their GP.

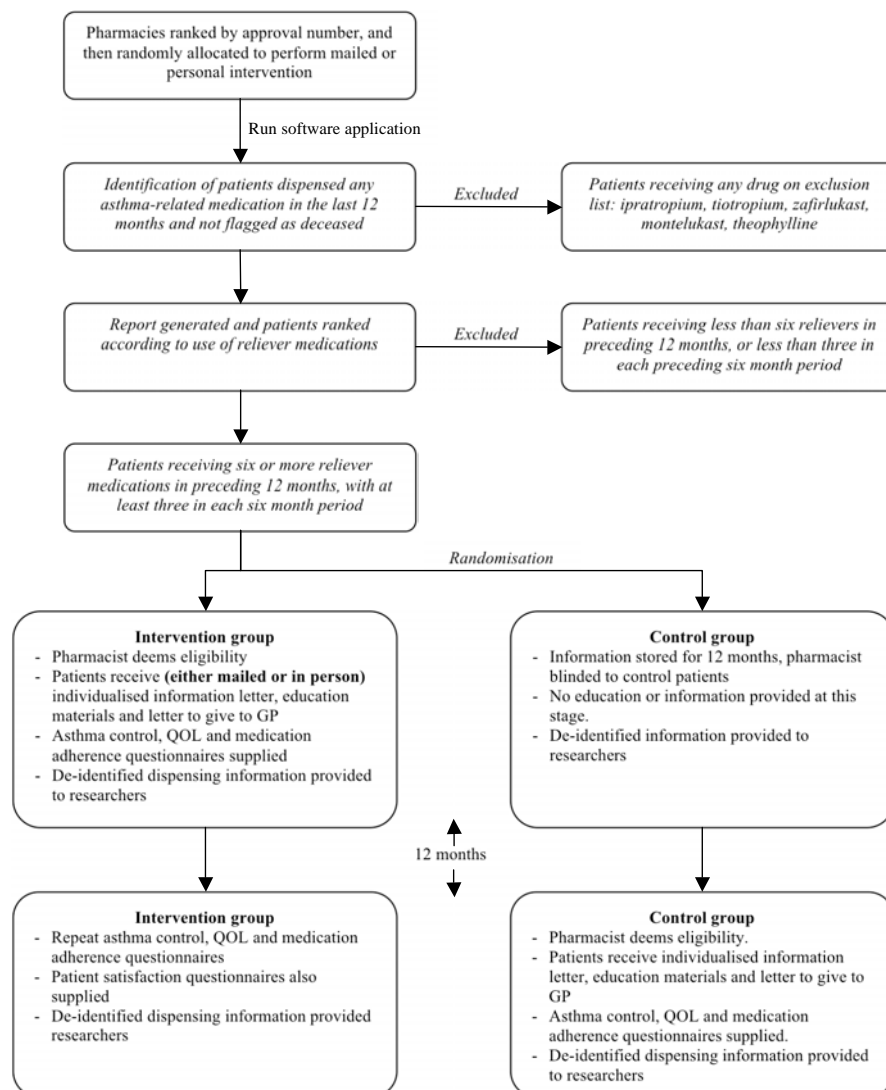
Control patients will receive usual care until follow-up, 12 months later. At this time they will receive an intervention pack and all intervention patients will receive repeat asthma-related questionnaires. Changes in asthma medication usage and questionnaire scores will be examined. Patient, pharmacist and GP satisfaction with the program will also be assessed. A pilot study demonstrated major improvements in the use of preventer medication at follow-up, and GPs, pharmacists and patients were highly satisfied with the intervention.

All participating community pharmacists will be provided with the study's key outcomes. It is intended that the results of the study will not only improve the management of asthma, but also demonstrate the most effective level of intervention required to reach that outcome. The project will also trial a valuable new role for community pharmacists - assisting in the detection of suboptimal use of medicines, including poor adherence to therapy, with the aid of information technology. Importantly, the solution requires minimal training and time commitments from pharmacists, and will be easily incorporated into busy community

This project is funded by the Pharmacy Guild of Australia Fourth Community Pharmacy Agreement Research and Development Program via an Investigator Initiated Grant



Pharmacy dispensing records to identify and educate patients with suboptimal asthma management



Key:
Project methods
Program algorithm

This project is funded by the Pharmacy Guild of Australia Fourth Community Pharmacy Agreement Research and Development Program via an Investigator Initiated Grant

Appendix 12. Pharmacist expression of interest form



Improving the management of asthma

Attention: Bonnie Bereznicki

- ☐ Yes, our pharmacy uses Fred Dispense, and we are willing to participate in the project, *Pharmacy dispensing records to identify and educate patients with suboptimal asthma management*, being conducted by the Tasmanian School of Pharmacy. Please contact us to discuss the details further.
- ☐ Sorry, we do not use Fred Dispense
- ☐ Sorry, we use Fred Dispense but don't feel able to participate in this project.

Pharmacist Name:

Pharmacy Name:

Pharmacy Address:

Pharmacy Phone:

Pharmacy Fax:

Signature of pharmacist Date.....

Please return this form to the Tasmanian School of Pharmacy in the reply paid envelope provided or by faxing it to us on 6226 7627.

Private Bag 83 Hobart
Tasmanian, Australia 7001
Telephone 6227 2191
Facsimile 6226 7627
Bonnie.Bereznicki@utas.edu.au

Appendix 13. GP project information sheet

Improving the control of asthma

GENERAL PRACTITIONER PROJECT INFORMATION SHEET

Why this project is needed

One of the major contributing factors to both morbidity and mortality of patients with asthma is their over-reliance on reliever medication, and under-use of preventive medication. A number of studies have shown that a high usage of reliever medication, relative to preventer medication, is associated with poorer clinical outcomes in asthma. With over 2 million Australians affected by asthma and only 14% of patients indicating regular use of preventive medication, we are seeking your assistance.

About this project

The project is being conducted by the University of Tasmania's School of Pharmacy with the help of selected pharmacies in Tasmania. A software program has been developed, which enables pharmacists to identify patients with asthma whose control may be suboptimal. Patients who receive six (6) or more reliever medications dispensed from the pharmacy in the last 12 months will be identified. Patients who are likely to have chronic obstructive pulmonary disease (i.e. receiving anticholinergic bronchodilators) will be excluded.

Patients are given educational material (developed by the Asthma Foundation) from the pharmacy and advised to seek a review of their asthma management from their GP. In order to help us learn more about how asthma affects people in the community, patients will also be asked to complete surveys about their asthma. Patient and GP surveys will be used to evaluate uptake and effectiveness of the intervention program.

The project has the support and involvement of the Tasmanian Divisions of General Practice.

Special note on privacy

Please be assured that your patient's identity has not been released to the University. No one at the University can identify the information that you or your patients provide; the survey forms are anonymous. No identifying information relating to patients, doctors or pharmacists will be disseminated. All project results will be de-identified and pooled for statistical analysis prior to a final report and publication.

Contact Information

If you have any concerns or queries about the project, please contact your local participating pharmacist, or Bonnie Bereznicki at the Tasmanian School of Pharmacy on telephone 6226 2191 or email bonnie.bereznicki@utas.edu.au.

The project has received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee. If you have any concerns of an ethical nature or complaints about the manner in which the project is conducted, you may contact the Executive Officer of the Tasmanian Human Research Ethics Committee (Tasmania) Network on 6226 7479 or human.ethics@utas.edu.au. You will need to quote ethics reference number H9823.

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia



Appendix 14. MedeMine-for-Asthma instructions for researchers

Pharmacy dispensing records to identify and educate patients with suboptimal asthma management

Instructions for installing and running MedeMine

Step 1. Obtain a portable copy of the MedeMine program

Download the updated version of MedeMine from:

<http://www.pharmacy.utas.edu.au/UMORE/downloads/Medeminev2.1.24.exe>

This icon will appear on your desktop. It is the installation package.

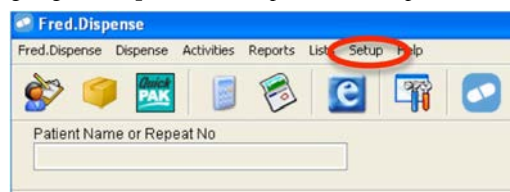


Medeminev2.1
.24

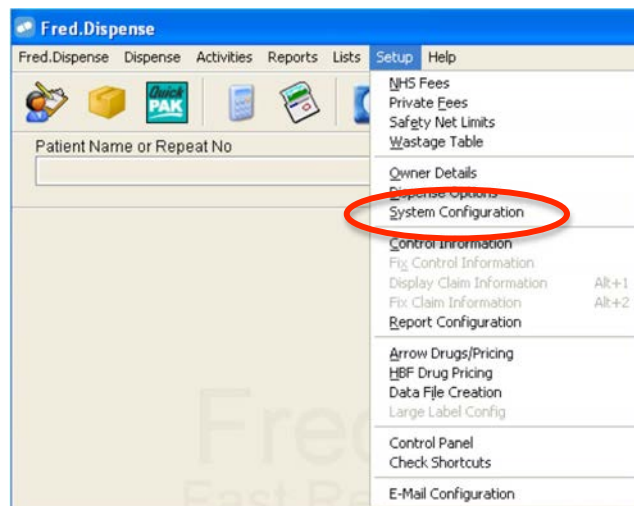
Copy this icon to your USB device.

Step 1. Locate the Fred Server

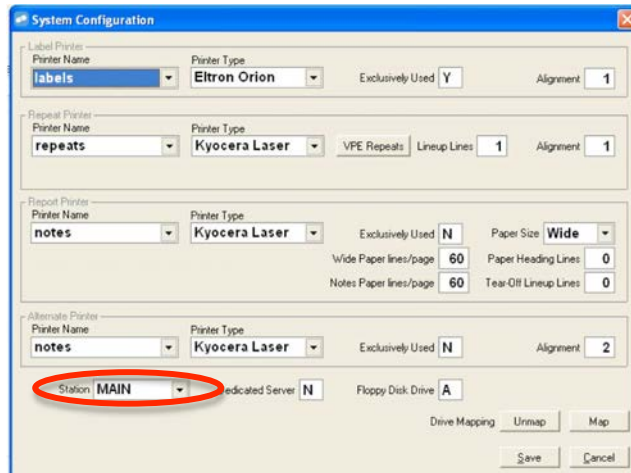
If the pharmacist is unsure which computer is the Fred Server, you can check in Fred, by going to **Setup** (one of the options at the top of the main Fred screen):



Select **System Configuration**:



If you are using the Fred Server, the **Station** will be **MAIN**, if you are not at the Fred Server, the **Station** will be **TERMINAL**:



Step 3. Install MedeMine

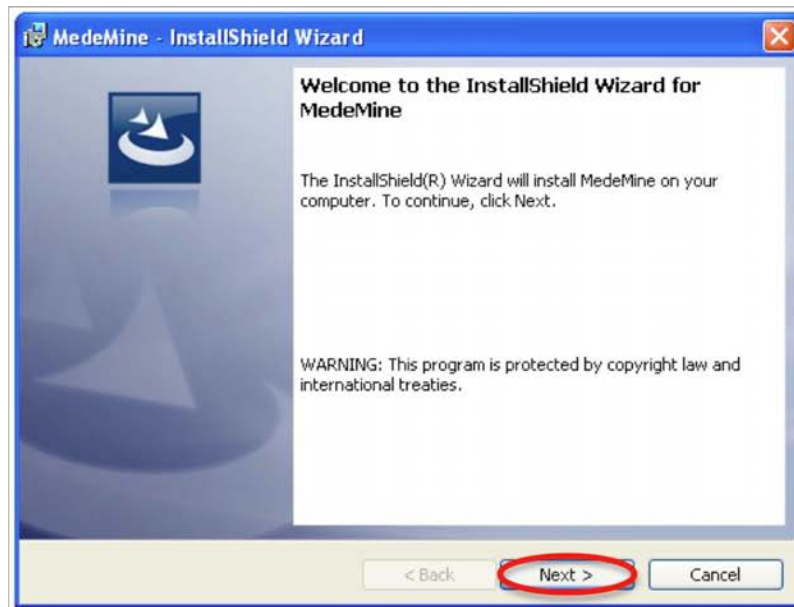
Plug your USB device into the Fred Server computer.

Copy the installation package from your USB device to the Fred Server's desktop. Double-click on the installation package icon to start the installation.

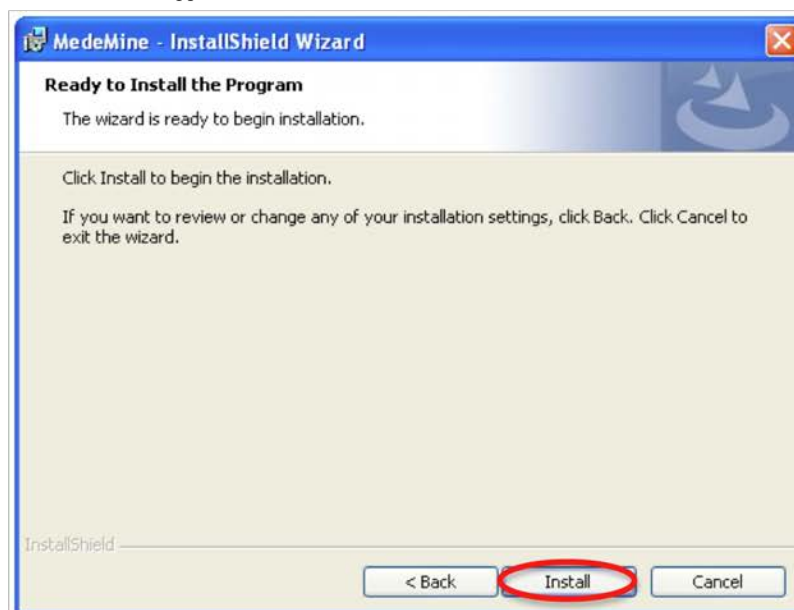
This screen will appear. Please wait.



Once this screen appears, click **Next**.



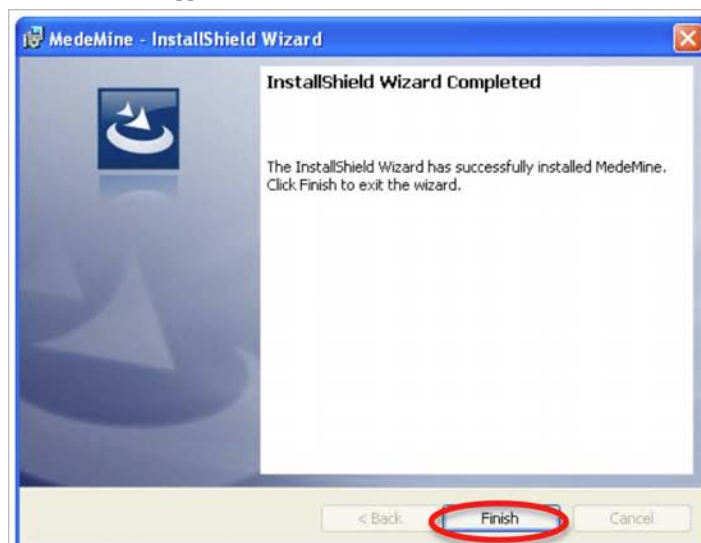
Once this screen appears, click **Install**.



This screen will then appear. Please wait.



Once this screen appears, click **Finish**.

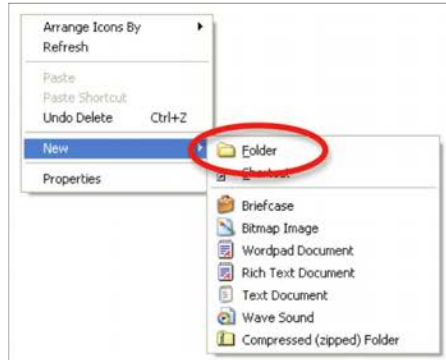


The MedeMine program is now installed. This icon will now appear on the desktop:



Step 3. Tidy-up the desktop

Right-click to create a new Folder on the desktop.



Name this folder **MedeMine**.



Place the Installation Package and the MedeMine shortcut in the MedeMine Folder.



Step 4. Run the MedeMine program

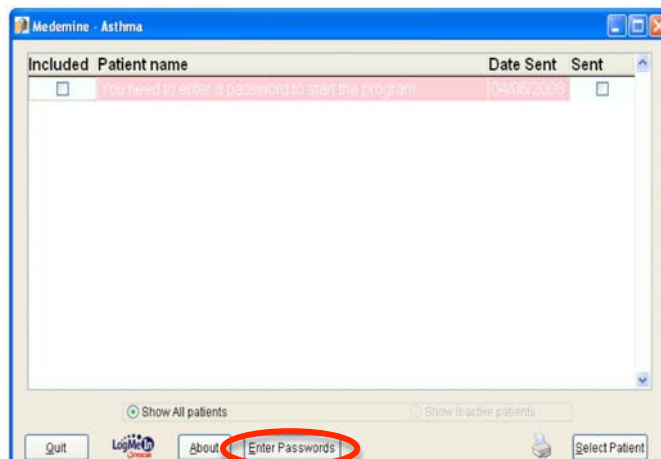
Double click on the **MedeMine** icon inside the MedeMine folder.



You will see the first screen:



After a brief pause you will see this screen. Click **Enter Passwords**.

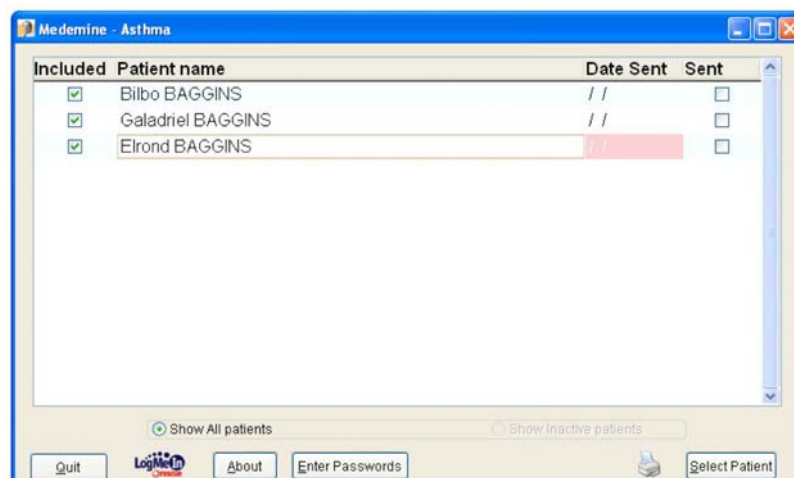


Enter the following password:

bAnan4 [bAnan(four)] for pharmacies randomised to type 1 (mailed) intervention, OR
0rag3s [(zero)rang(three)s] for pharmacies randomised to type 2 (face-to-face) intervention.

(Note: the password only has to be entered when the program is opened for the first time)

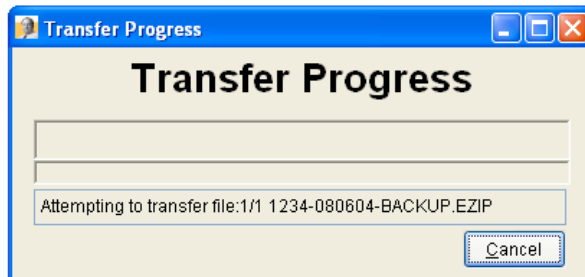
The list of intervention patients will now appear.



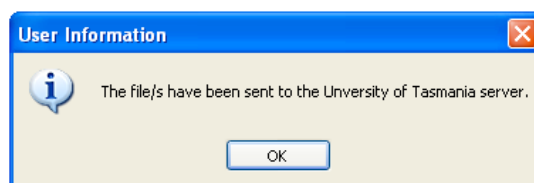
Refer to the Pharmacist's Instructions. Go through these instructions with the pharmacist to ensure that they are confident with how to use the MedeMine program. Once the pharmacist is confident, you can close the MedeMine program.

Step 5. Close the MedeMine program

When the MedeMine program closes, this screen will appear:



When this is complete, this screen will appear.



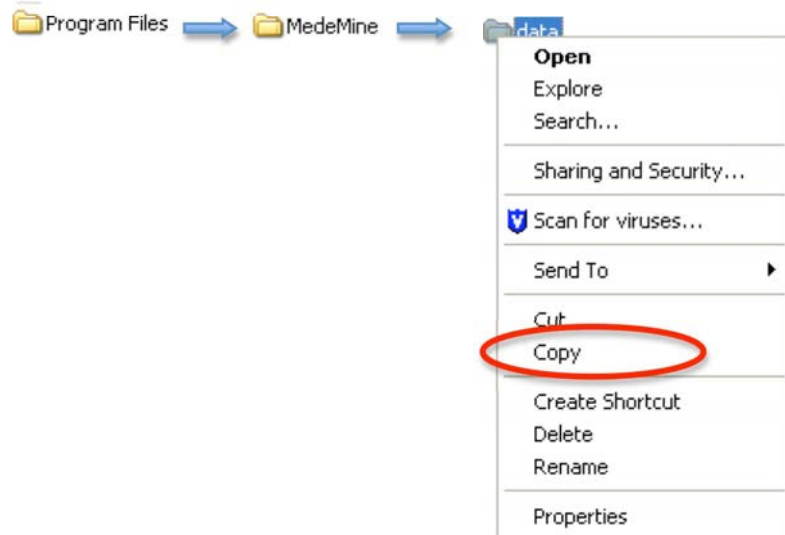
Step 6. Obtain a back-up of the de-identified dispensing data

Insert your USB stick into the Server's USB drive.

Go to **My Computer** and open the **C-drive**.

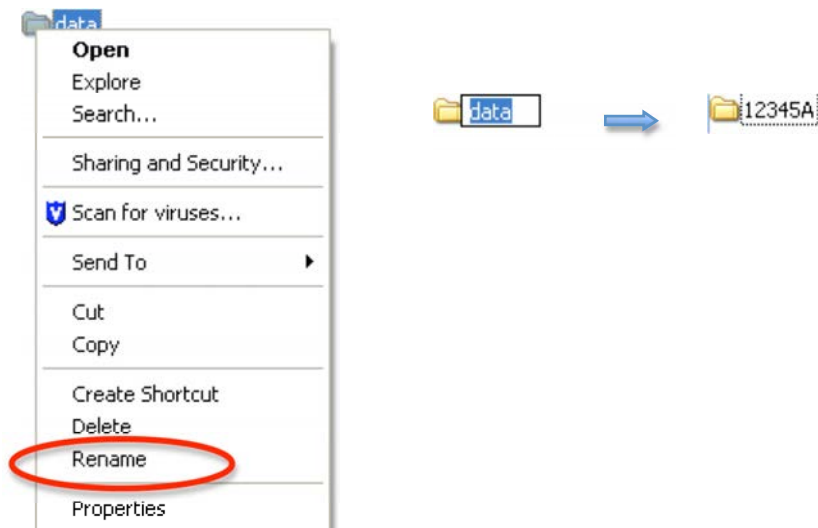


Locate and double-click on **Program Files**. Locate and double click on **MedeMine**.
Locate and right-click on the **Data** folder, select **Copy**.



Copy the **Data** folder to your USB device

Right-click to re-name the **Data** folder with the pharmacy's approval number. This will aid in keeping track of which data comes from which pharmacy.



Eject your USB device. You are now ready to visit the next pharmacy.

Appendix 15. Pharmacist instructions for mailed intervention

Pharmacy dispensing records to identify and educate patients with suboptimal asthma management

Intervention type I

Your simple step-by step instructions to successfully participate in this project

1. Install the MedeMine program on the Fred server
2. Run the program to identify eligible patients
3. Exclude any intervention patients as necessary
4. Mail packs to each included intervention patient
5. Document any feedback
6. Six-week follow-up
7. Run the program again in 12 months
8. Mail follow-up letter and surveys to each included intervention patient
9. Exclude any control patients as necessary
10. Mail packs to each included control patient

Step 1. Install the MedeMine program on the Fred server

Your Project Officer will install the MedeMine program on your Fred Server. This is usually the main Fred Computer and will be the computer you run monthly updates on.

Once the program is installed, the Project Officer will place it in a folder on your desktop:



Step 2. Run the program to identify eligible patients

Run the MedeMine program by double-clicking on the **MedeMine** icon, located in the MedeMine folder on the desktop of your Fred Server.



You will see the first screen:



After a brief pause you will see the main window:



This is the list of patients identified by the software as eligible for inclusion into the study. That is, patients who have received 6 or more canisters of asthma reliever medication (salbutamol/terbutaline) in the past 12 months, with at least 3 canisters supplied in each six-month period.

Step 3. Exclude any intervention patients as necessary

For each patient identified by the software, you will need to exclude any who meet the pre-defined exclusion criteria.

Highlight a patient's name by a single left-click, and then left-click on **Select Patient**, which you will see in the bottom right hand corner of the screen OR

Double left-click on a patient's name.

This will open up an individual patient's file as seen below:

Disp	Drug Name	Qty	Directions	Dec	Rpt	Dp	\$	By
23/04	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	3	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8883
27/03	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	2	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8881
28/02	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	1	6.50	NB
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8879
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU					8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	500mcg 60d		mouth TWICE a day **REGU					8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-AERO 200 Dose		TWO puffs by mouth every					8873
28/11	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	4	6.40	DC

This screen uses tabs to show more information on a single screen.

For more information on these tabs, please refer to the additional notes on the next page.

A patient can be excluded at two distinct time points: before the pack is sent to the patient, or after the pack is sent. To EXCLUDE a patient, select a reason from the **Reason for Exclusion** drop-down menu - this is located in the top right-hand corner of the screen.

For each patient identified by the software, you will need to exclude any who meet the pre-defined exclusion criteria, listed in the drop-down menu, ABOVE the black line:

- Too confused
- Deceased
- Patient has COPD
- Nursing home resident
- May cause undue distress
- Under 18 years old
- If you have another reason to exclude the patient select **other....** and type the reason.

Date	Drug Name	Dose	Directions	STOA	DC
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	5	6.50 DC
2008	MET-ABRO 200 Dose		TWO puffs by mouth every		8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA 1	4.90 DC
2007	500mcg		mouth TWICE a day **REGU		8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA 5	4.90 DC
2007	50mcg 60d		mouth TWICE a day **REGU		8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA 5	6.40 DC
2007	MET-ABRO 200 Dose		TWO puffs by mouth every		8873

Once you have selected a reason for exclusion for a patient, you will be directed to the **Extra Information** screen. If you have any information to add as to why the patient should be excluded, you can free-type in the boxes within this screen. Otherwise, just click **Close**. This will take you back to the list of patients.

Once you have reviewed each patient on the list to determine their eligibility, you are ready to print the letters and surveys

Additional notes - Tabs

The first three tabs (**Asthma-related Dispensings**, **Collated History** and **All Dispensing History**) are ways of looking at the patient's history. For the first three tabs you can vary the amount of history you can see by selecting a time frame from the **Months History to display** option group (**1,3,6,9,12** or **all**) – this is located immediately above the tabs.

Asthma-related dispensings

This is a list of the patient's history that only shows you asthma-related medicines. You can show more or less history by clicking on the **Months History to display** option group.

Collated History

This tab will show each generic drug/ form/ strength the patient had dispensed, in order of the number of supplies in the time period specified. For example if the patient had one supply of Ventolin[®] MDI 100mcg and one supply of Asmol[®] MDI 100mcg there would be two supplies of Salbutamol MDI 100mcg. The directions shown are of the last dispensing, and the date shown is the last dispensing date. You can show more or less history by clicking on the month in the **Months History to display** option group.

All Dispensing History

All dispensing history is similar to the history you see in Fred dispense except patient notes are *not* shown and cancelled scripts *are* shown (in grey type). You can show more or less history by clicking on the month in **Months History to display** option group.

Extra Information

Please refer to Step 5 for information about this Tab.

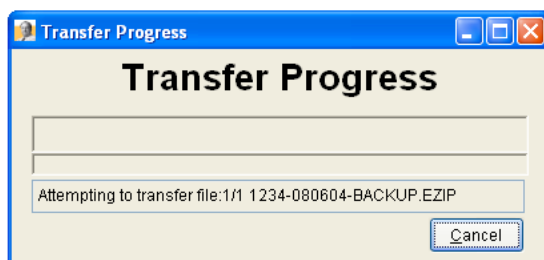
Additional Notes - Internet

The program requires an active Internet connection to send information to the server at the University of Tasmania.

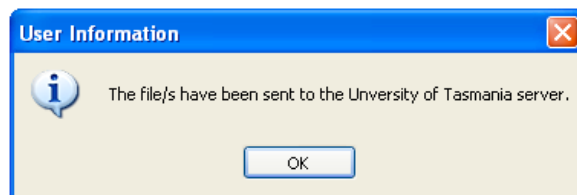
Only de-identified and encrypted information is sent to the secure server. The program uses a 1024 bit key to securely send information.

If an Internet connection is not available the program will prompt you to connect to the Internet. If you do not connect to the Internet the program will still work, and will send the information using the Internet at a later time.

Every time the MedeMine program closes, this screen will appear. This shows that the de-identified and encrypted information is being sent to the secure server at the University.



When this is complete, this screen will appear.



Step 4. Mail packs to each included intervention patient

The first thing you need to do is to check that the printer is set up correctly. The program should have automatically selected the printer that you normally print notes or CMIs to.

To check if the program has selected the correct printer; click on the picture of the printer as shown below (located on the bottom right-hand side of the screen showing the list of patients) and select the printer that you normally print A4 pages to with Fred.



Once the correct printer is selected, click on the **Print Letters** button (located on the bottom right-hand side of the screen showing the list of patients). Please enter your name when prompted. This will print the materials for each patient that you have not excluded.

Collate the printed material as follows:

- The first page is a personalised letter to the patient explaining that your pharmacy is participating in the research project. Please sign the bottom of this letter. This letter is to be placed in an A4 envelope provided by you Project Officer. This envelope will already contain an educational brochure about asthma ('Asthma: the basic facts').
- All documents with a small 'A' in the bottom right hand corner are to be placed in 'Envelope A – Information for your doctor'. There should be a letter to the GP and an 'Evaluation by General Practitioners' survey. Please sign the bottom of the GP letter. Envelope A will already contain a General Practitioner Project Information Sheet and a reply paid envelope for the GPs to return their completed anonymous survey to the University.
- All documents with a small 'B' in the bottom right hand corner are to be placed in 'Envelope B – Please join our survey'. There will be three patient surveys titled 'Patient Asthma Survey (Quality of Life)', 'Patient Asthma Survey (Asthma Control)', and 'Patient Asthma Survey (Medication Adherence)'. Envelope B will already contain a Survey Information Sheet for patients and a reply paid envelope for the patients to return their completed anonymous surveys to the University.
- Place envelope A and envelope B inside the A4 envelope.

Address labels for the A4 envelopes can be printed by placing Avery L7162 label sheets in the A4 paper tray of your notes printer. Select **Print Labels**.

Alternatively, address labels for the A4 envelopes can be printed using Fred.

Send the packs to all included intervention patients with \$1.00 postage. You will be reimbursed for the postage costs at the time of the first payment (see Step 6).

Step 5. Document any feedback

In the next six weeks if a patient who was sent a pack contacts you about the project we would encourage you to enter information into the **Extra Information** tab of the patient details screen. This tab is used provide further feedback to the researchers about the project.

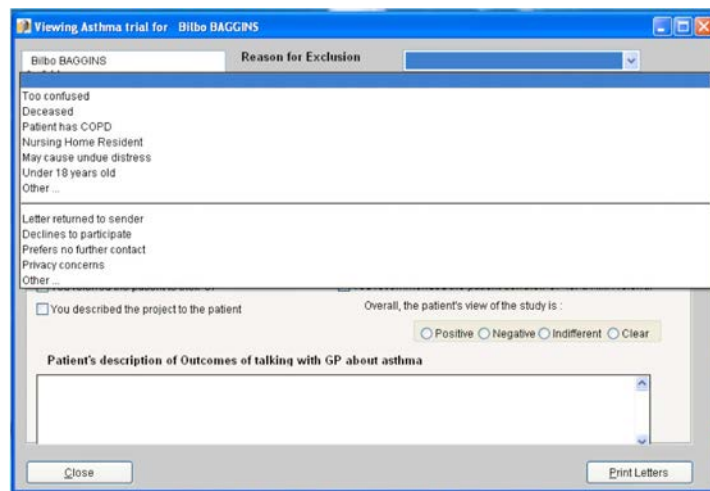
There are two basic types of feedback;

- feedback from the patient about how they feel, and
- feedback the patient relays to you about how the GP feels.

The screenshot shows a software window titled "Viewing Asthma trial for Bilbo BAGGINS". It contains a form for entering patient feedback. The "Extra Information" tab is active. The form includes fields for "Reason for Exclusion", "Initial Letter Printed on:", "Second Letter Printed on:", and "Seen by GP". Below these are tabs for "Asthma-related Dispensings", "Collated History", "All Dispensing History", and "Extra Information". The "Extra Information" tab contains a section for "Patient's feedback about project" with checkboxes for "You counselled the patient on their inhaler technique", "You referred the patient to their GP", "You described the project to the patient", "You recommended the patient ask their GP for an asthma plan", and "You recommended the patient ask their GP for a HMR referral". There is also a section for "Overall, the patient's view of the study is:" with radio buttons for "Positive", "Negative", "Indifferent", and "Clear". At the bottom, there is a section for "Patient's description of Outcomes of talking with GP about asthma" with a text area. Buttons for "Close" and "Print Letters" are at the bottom right.

Now is also the time you can exclude patients from further participation in the project, if necessary. Any secondary exclusion reasons can be chosen from the **Reason for exclusion** drop-down menu - this is located in the top right hand corner of the screen. The secondary exclusion reasons are those BENEATH the black line, and include

- Letter returned to sender
- Declines to participate
- Prefers no further contact
- Privacy concerns
- If you have another reason to exclude the patient select **other....** and type the reason.



The first secondary exclusion reason lets the researchers know to exclude the patient from analysis because if the intervention pack was returned to sender, the patient would not have received an intervention.

The other secondary exclusion reasons ensure the patient is excluded from follow-up contact at 12 months.

Step 6. Six-week follow-up

After six weeks have elapsed, your local project officer will arrange a time to visit your pharmacy. At this point you will given instructions on how to claim your first payment, which will include reimbursement for postage costs. You will also be asked to complete a short survey regarding your perceptions of the project. You have now finished the first part of the project.

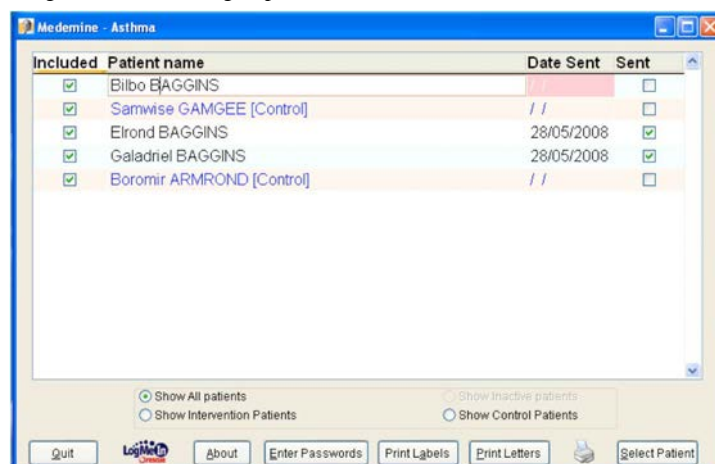
Over the next 12 months if a patient who was sent a pack contacts you about the project we would encourage you to enter information into the **Extra Information** tab of the patient details screen.

Step 7. Run the program again in 12 months

After 12 months have elapsed, the second phase of the trial will begin.

- Your local project officer will arrange a time to visit your pharmacy. You will be provided with a password.
- Run the MedeMine program again and left-click on the **Enter passwords** button and enter the password you were given.

After you have entered the correct password the program will reveal the names of the patients assigned to the control group.



Step 8. Mail follow-up letter and surveys to each included intervention patient

Select **Show Intervention Patients**

- This will give you a list of all intervention patients who were originally sent a pack and not subsequently excluded from the trial.

Select **Print Letters**

- Please enter your name when prompted. The program will print four surveys and a cover letter for each intervention patient who was originally sent a pack and not subsequently excluded from the trial.
- Please sign the cover letter, and place the letters and surveys in the envelopes provided by your Project Officer. This envelope will already contain a reply paid envelope for the patients to return their completed anonymous surveys to the University.
- Send the letters and surveys to all included intervention patients with \$1.00 postage.

Step 9. Exclude any control patients as necessarySelect **Show Control Patients**

- This will give you a list of patients who were originally identified as receiving 6 or more canisters of asthma reliever medication (salbutamol/terbutaline) the 12 months prior to the project start date, and who were assigned to the control group.
- You now need to exclude any of the control patients who meet the pre-defined exclusion criteria. Do this using the same method that was used at the beginning of the trial for the Intervention Patients. (See Step 3)
- Highlight a Control Patient's name by a single left-click, and then left-click on **Select Patient**, which you will see in the bottom right hand corner of the screen.
- OR
- Double left-click on the control patient's name.
- To **EXCLUDE** a control patient, select a reason from the **Reason for exclusion** drop-down menu - this is located in the top right hand corner of the screen.
- For each patient identified by the software, you will need to exclude any who meet the pre-defined exclusion criteria, listed in the drop-down menu, **ABOVE** the black line (too confused, deceased, patient has COPD, nursing home resident, may cause undue distress, under 18 years old, or other).

All included control patients will now be sent an intervention pack. Therefore, you will need to exclude any control patients who no longer qualify for an intervention pack, that is, if they have received less than 6 canisters of asthma reliever medication in the past 12 months).

- Select a patient, click on **Collated History** and select 12 months. Exclude any control patients who have received less than 6 relievers in the last 12 months. To exclude such patients from receiving an intervention pack, select **Other....** and type "<6 relievers".

Viewing Asthma trial for Samwise GAMGEE

Samwise GAMGEE
Bag End
The Shire 7000

Reason for Exclusion [Dropdown menu]

Initial Letter Printed on: / / .. AM
Second Letter Printed on: / / .. AM
Seen by GP ☐

Months History to display ☐ 1 ☐ 3 ☐ 6 ☐ 9 ☒ 12 ☐ All

#	DISP	Drug name	Directions	last Disp
11	Celecoxib CAP 200mg (30)	Take ONE capsule daily immediately after food	22/04 2008	
11	Eformoterol T-HALER 6mcg (1)	Inhale ONE dose by mouth TWICE a day as directed by your doctor	22/04 2008	
11	Fluticasone A-HALER 250mcg (1)	Inhale ONE dose by mouth TWICE a day *Rinse mouth out with water after use	22/04 2008	
11	Roxithromycin TAB 300mg (5)	Take ONE tablet with a glass of water daily about 15 mins before food until fin	26/04 2008	
10	Salbutamol Cfc Free MET-AERO 200 Dose (2)	Shake well and inhale TWO puffs by mouth every FOUR hours when required	22/04 2008	
9	Codeine & Paracetamol TAB 500-	Take HALF a tablet FOUR times a day when required as directed	22/04 2008	
9	Ranitidine TAB 150mg (60)	Take ONE tablet TWICE a day	22/04 2008	
7	Paracetamol TAB	Take TWO tablets every FOUR hours when	22/04	

Close **Print Letters**

Once you have reviewed each control patient on the list to determine their eligibility, you are ready to print the letters and surveys

Step 10. Mail packs to each included control patient

On the screen showing the list of patients, select **Show Control Patients** and click on the **Print Letters** button. Please enter your name when prompted. This will print the materials for each control patient that you have not excluded.

Collate the printed material as follows:

- The first page is a personalised letter to the patient explaining that the pharmacy is participating in the research project. Please sign the bottom of this letter. This letter is to be placed in an A4 envelope. This envelope will already contain an educational brochure about asthma ('Asthma: the basic facts').
- All documents with a small 'A' in the bottom right hand corner are to be placed in 'Envelope A – Information for your doctor'. There should be a letter to the GP and an 'Evaluation by General Practitioners' survey. This envelope will already contain a General Practitioner Project Information Sheet and a reply paid envelope for the GPs to return their completed survey in.
- All documents with a small 'B' in the bottom right hand corner are to be placed in 'Envelope B – Please join our survey'. There will be three patient surveys titled 'Patient Asthma Survey (Quality of Life)', 'Patient Asthma Survey (Asthma Control)', and 'Patient Asthma Survey (Medication Adherence)'. Envelope B will already contain a Survey Information Sheet and a reply paid envelope for the patients to return their completed surveys in.
- Place envelope A and envelope B inside the A4 envelope.

Address labels for the A4 envelopes can be printed by placing Avery L7162 label sheets in the A4 paper tray of your notes printer. Select **Print Labels**.

Alternatively, address labels for the A4 envelopes can be printed using Fred.

Send the packs to all included intervention patients with \$1.00 postage.

At this point you will given instructions on how to claim your final payment, which will include reimbursement for postage costs.

You have now finished the project.

Thankyou for your participation!

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Appendix 16. Pharmacist instructions for face-to-face intervention

Pharmacy dispensing records to identify and educate patients with suboptimal asthma management

Intervention type II

Your simple step-by step instructions to successfully participate in this project

1. Install the MedeMine program on the Fred server
2. Run the program to identify eligible patients
3. Exclude any intervention patients as necessary
4. Hand-out packs to each included intervention patient
5. Document any feedback
6. Six-week follow-up
7. Run the program again in 12 months
8. Mail follow-up letter and surveys to each included intervention patient
9. Exclude any control patients as necessary
10. Mail packs to each included control patient

Step 1. Install the MedeMine program on the Fred server

Your Project Officer will install the MedeMine program on your Fred Server. This is usually the main Fred Computer and will be the computer you run monthly updates on.

Once the program is installed, the Project Officer will place it in a folder on your desktop:



Step 2. Run the program to identify eligible patients

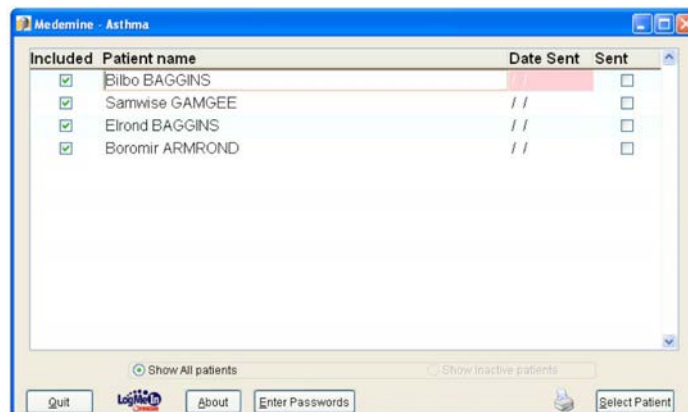
Run the MedeMine program by double-clicking on the **MedeMine** icon, located in the MedeMine folder on the desktop of your Fred Server.



You will see the first screen:



After a brief pause you will see the main window:



This is the list of patients identified by the software as eligible for inclusion into the study. That is, patients who have received 6 or more canisters of asthma reliever medication (salbutamol/terbutaline) in the past 12 months, with at least 3 canisters supplied in each six-month period.

Step 3. Exclude any intervention patients as necessary

For each patient identified by the software, you will need to exclude any who meet the pre-defined exclusion criteria.

Highlight a patient's name by a single left-click, and then left-click on **Select Patient**, which you will see in the bottom right hand corner of the screen OR

Double left-click on a patient's name.

This will open up an individual patient's file as seen below:

Disp	Drug Name	Qty	Directions	Doc	Rpt	Dp	\$	By
23/04	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	3	6.50	DC
2008	MET-ABRO 200 Dose		TWO puffs by mouth every					8883
27/03	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	2	6.50	DC
2008	MET-ABRO 200 Dose		TWO puffs by mouth every					8881
28/02	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	1	6.50	NB
2008	MET-ABRO 200 Dose		TWO puffs by mouth every					8879
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-ABRO 200 Dose		TWO puffs by mouth every					8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU					8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	50mcg 60d		mouth TWICE a day **REGU					8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-ABRO 200 Dose		TWO puffs by mouth every					8873
22/11	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	4	6.40	DC

This screen uses tabs to show more information on a single screen.

For more information on these tabs, please refer to the additional notes on the next page.

A patient can be excluded at two distinct time points: before the pack is sent to the patient, or after the pack is sent. To EXCLUDE a patient, select a reason from the **Reason for Exclusion** drop-down menu - this is located in the top right-hand corner of the screen.

For each patient identified by the software, you will need to exclude any who meet the pre-defined exclusion criteria, listed in the drop-down menu, ABOVE the black line:

- Too confused
- Deceased
- Patient has COPD
- Nursing home resident
- May cause undue distress
- Under 18 years old
- If you have another reason to exclude the patient select **other** and type the reason.

Date	Drug	Dose	Directions	STOA	5	6	6.50 DC
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50 DC
2008	MST-ABRO 200 Dose		TWO puffs by mouth every				8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90 DC
2007	500mcg		mouth TWICE a day **REGU				8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90 DC
2007	50mcg 60d		mouth TWICE a day **REGU				8876
31/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40 DC
2007	MST-ABRO 200 Dose		TWO puffs by mouth every				8873

Once you have selected a reason for exclusion for a patient, you will be directed to the **Extra Information** screen. If you have any information to add as to why the patient should be excluded, you can free-type in the boxes within this screen. Otherwise, just click **Close**. This will take you back to the list of patients.

Once you have reviewed each patient on the list to determine their eligibility, you are ready to print the letters and surveys

Additional notes - Tabs

The first three tabs (**Asthma-related Dispensings**, **Collated History** and **All Dispensing History**) are ways of looking at the patient's history. For the first three tabs you can vary the amount of history you can see by selecting a time frame from the **Months History to display** option group (**1,3,6,9,12** or **all**) – this is located immediately above the tabs.

Asthma-related dispensings

This is a list of the patient's history that only shows you asthma-related medicines. You can show more or less history by clicking on the **Months History to display** option group.

Collated History

This tab will show each generic drug/ form/ strength the patient had dispensed, in order of the number of supplies in the time period specified. For example if the patient had one supply of Ventolin[®] MDI 100mcg and one supply of Asmol[®] MDI 100mcg there would be two supplies of Salbutamol MDI 100mcg. The directions shown are of the last dispensing, and the date shown is the last dispensing date. You can show more or less history by clicking on the month in the **Months History to display** option group.

All Dispensing History

All dispensing history is similar to the history you see in Fred dispense except patient notes are *not* shown and cancelled scripts *are* shown (in grey type). You can show more or less history by clicking on the month in **Months History to display** option group.

Extra Information

Please refer to Step 5 for information about this Tab.

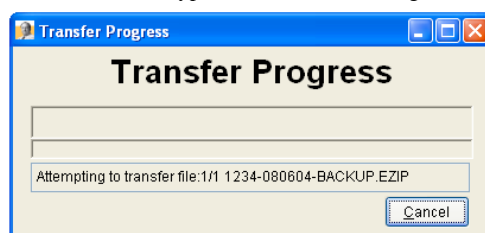
Additional Notes - Internet

The program requires an active Internet connection to send information to the server at the University of Tasmania.

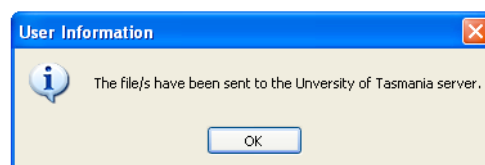
Only de-identified and encrypted information is sent to the secure server. The program uses a 1024 bit key to securely send information.

If an Internet connection is not available the program will prompt you to connect to the Internet. If you do not connect to the Internet the program will still work, and will send the information using the Internet at a later time.

Every time the MedeMine program closes, this screen will appear. This shows that the de-identified and encrypted information is being sent to the secure server at the University.

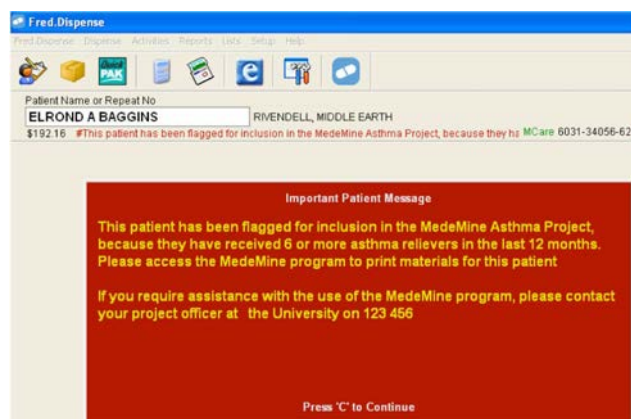


When this is complete, this screen will appear.



Step 4. Hand-out packs to each included intervention patient

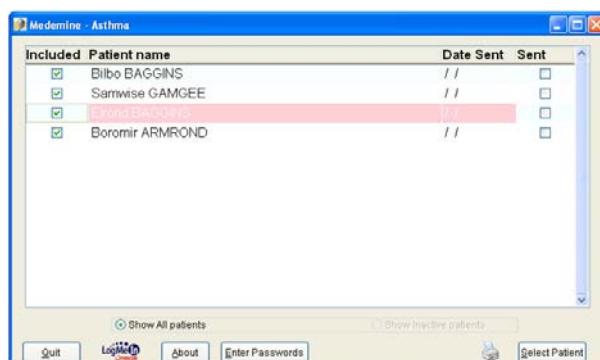
The next time you use Fred to dispense a medication for an included intervention patient, an alert flag will pop up, reminding you to access the MedeMine program to print materials for the patient and provide them with an intervention pack.



Open the MedeMine program by double-clicking on the MedeMine icon, located in the MedeMine folder on the desktop of your Fred Server.



After a brief pause you will see the main window:



The first thing you need to do is to check that the printer is set up correctly. The program should have automatically selected the printer that you normally print notes or CMI's to.

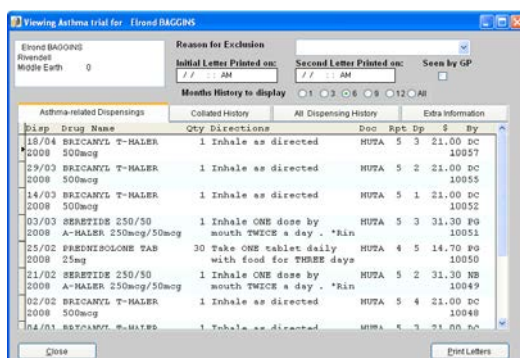
To check if the program has selected the correct printer; click on the picture of the printer as shown below (located on the bottom right-hand side of the screen showing the list of patients) and select the printer that you normally print A4 pages to with Fred.



Once the correct printer is selected, highlight a patient's name by a single left-click, and then left-click on 'Select Patient', which you will see in the bottom right hand corner of the screen.
OR

Double left-click on a patient's name.

This will open up an individual patient's file as seen below:



Click on the **Print Letters** button, located on the bottom right-hand side of the screen. Please enter your name when prompted. This will print the materials for the patient.

Collate the printed material as follows:

- The first page is a personalised letter to the patient explaining that your pharmacy is participating in the research project. Please sign the bottom of this letter. This letter is to be placed in an A4 envelope provided by you Project Officer. This envelope will already contain an educational brochure about asthma ('Asthma: the basic facts').
- All documents with a small 'A' in the bottom right hand corner are to be placed in 'Envelope A – Information for your doctor'. There should be a letter to the GP and an 'Evaluation by General Practitioners' survey. Please sign the bottom of the GP letter. Envelope A will already contain a General Practitioner Project Information Sheet and a reply paid envelope for the GPs to return their completed anonymous survey to the University.
- All documents with a small 'B' in the bottom right hand corner are to be placed in 'Envelope B – Please join our survey'. There will be three patient surveys titled 'Patient Asthma Survey (Quality of Life)', 'Patient Asthma Survey (Asthma Control)', and 'Patient Asthma Survey (Medication Adherence)'. Envelope B will already contain a Survey Information Sheet for patients and a reply paid envelope for the patients to return their completed anonymous surveys to the University.
- Place envelope A and envelope B inside the A4 envelope.

Hand the A4 envelope to the patient.

Step 5. Document any feedback

In the next six weeks, continue to print and hand out the intervention packs to patients as they present to the pharmacy for prescriptions. If a patient who is given a pack talks you about the project we would encourage you to enter information into the **Extra Information** tab of the patient details screen. This tab is used provide further feedback to the researchers about the project.

There are two basic types of feedback;

- feedback from the patient about how they feel, and
- feedback the patient relays to you about how the GP feels.

Now is also the time you can exclude patients from further participation in the project, if necessary. Any secondary exclusion reasons can be chosen from the **Reason for exclusion** drop-down menu - this is located in the top right hand corner of the screen. The secondary exclusion reasons are those BENEATH the black line, and include

- Letter returned to sender (*not relevant to this type of intervention*)
- Declines to participate
- Prefers no further contact
- Privacy concerns
- If you have another reason to exclude the patient select **other....** and type the reason.

The screenshot shows a software window titled "Viewing Asthma trial for Etrond BAGGINS". It features a "Reason for Exclusion" dropdown menu. Below the menu, there is a list of exclusion reasons: "Too confused", "Deceased", "Patient has COPD", "Nursing Home Resident", "May cause undue distress", "Under 18 years old", and "Other ...". A horizontal line separates these from a second list: "Letter returned to sender", "Declines to participate", "Prefers no further contact", "Privacy concerns", and "Other". Below this, there is a checkbox labeled "You described the project to the patient". To the right, there is a section titled "Overall, the patient's view of the study is :" with radio buttons for "Positive", "Negative", "Indifferent", and "Clear". Below this is a section titled "Patient's description of Outcomes of talking with GP about asthma" with a text area. At the bottom of the window are "Close" and "Reprint Letters" buttons.

The secondary exclusion reasons ensure the patient is excluded from follow-up contact at 12 months.

Step 6. Six-week follow-up

After six weeks have elapsed, your local project officer will arrange a time to visit your pharmacy. At this point you will given instructions on how to claim your first payment, which will include reimbursement for postage costs. You will also be asked to complete a short survey regarding your perceptions of the project. You have now finished the first part of the project.

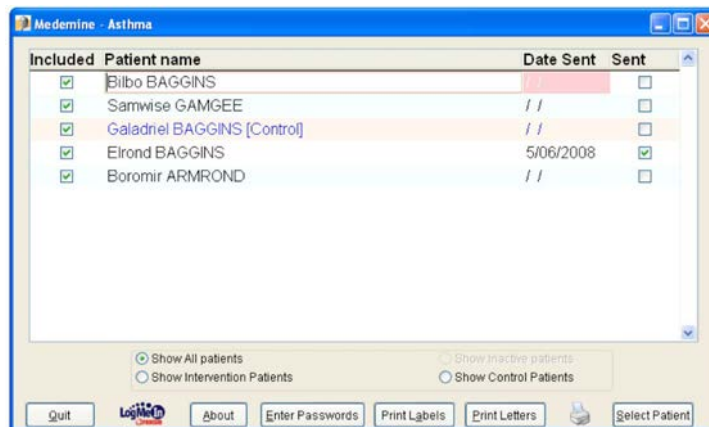
Over the next 12 months if a patient who was given a pack talks to you about the project we would encourage you to enter information into the 'Extra Information' tab of the patient details screen.

Step 7. Run the program again in 12 months

After 12 months have elapsed, the second phase of the trial will begin.

- Your local project officer will arrange a time to visit your pharmacy. You will be provided with a password.
- Run the MedeMine program again and left-click on the **Enter passwords** button and enter the password you were given.

After you have entered the correct password the program will reveal the names of the patients assigned to the control group.



Step 8. Mail follow-up letter and surveys to each included intervention patient

Select **Show Intervention Patients**

- This will give you a list of all intervention patients who were originally sent a pack and not subsequently excluded from the trial.

Select **Print Letters**

- Please enter your name when prompted. The program will print four surveys and a cover letter for each intervention patient who was originally sent a pack and not subsequently excluded from the trial.
- Please sign the cover letter, and place the letters and surveys in the envelopes provided by your Project Officer. This envelope will already contain a reply paid envelope for the patients to return their completed anonymous surveys to the University.
- Send the letters and surveys to all included intervention patients with \$1.00 postage.

Step 9. Exclude any control patients as necessarySelect **Show Control Patients**

- This will give you a list of patients who were originally identified as receiving 6 or more canisters of asthma reliever medication (salbutamol/terbutaline) the 12 months prior to the project start date, and who were assigned to the control group.
- You now need to exclude any of the control patients who meet the pre-defined exclusion criteria. Do this using the same method that was used at the beginning of the trial for the Intervention Patients. (See Step 3)
- Highlight a Control Patient's name by a single left-click, and then left-click on **Select Patient**, which you will see in the bottom right hand corner of the screen.
- OR
- Double left-click on the control patient's name.
- To **EXCLUDE** a control patient, select a reason from the **Reason for exclusion** drop-down menu - this is located in the top right hand corner of the screen.
- For each patient identified by the software, you will need to exclude any who meet the pre-defined exclusion criteria, listed in the drop-down menu, **ABOVE** the black line (too confused, deceased, patient has COPD, nursing home resident, may cause undue distress, under 18 years old, or other).

All included control patients will now be sent an intervention pack. Therefore, you will need to exclude any control patients who no longer qualify for an intervention pack, that is, if they have received less than 6 canisters of asthma reliever medication in the past 12 months).

- Select a patient, click on **Collated History** and select 12 months. Exclude any control patients who have received less than 6 relievers in the last 12 months. To exclude such patients from receiving an intervention pack, select **Other....** and type "<6 relievers".

Viewing Asthma trial for Galadriel BAGGINS

Galadriel BAGGINS
Elrond
Middle Earth 0

Reason for Exclusion: **Other....**

Initial Letter Printed on: / / : : AM Second Letter Printed on: / / : : AM Seen by GP ☐

Months History to display: ☐ 1 ☐ 3 ☐ 6 ☐ 9 ☒ 12 ☐ All

# DISP	Drug name	Directions	last Disp
10	Lercanidipine TAB 10mg (30)	Take ONE tablet daily **REGULAR DOSAGE IS ESSENTIAL**	14/04 2008
8	Salbutamol Cfc Free MET-AERO 200 Dose (2	Shake well and inhale TWO puffs by mouth every FOUR hours when required .	19/03 2008
7	Methyldopa TAB 250mg (100)	Take ONE tablet TWICE a day with food . *May cause dizziness when standing up qui	14/04 2008
5	Trimethoprim TAB 300mg (7)	Take ONE tablet daily with food until finished	07/04 2008
3	Hypromellose & Dextran EYE-DRP 15mL	Instil ONE drop in each eye when required - Discard contents 28 days after	14/04 2008
2	Cephalexin CAP 500mg (20)	Take ONE capsule THREE times a day until finished	14/04 2008
2	Paracetamol TAB 500mg (100)	Take TWO tablets FOUR times a day when required , *Maximum of EIGHT per day	12/11 2007
1	Betamethasone Hal	Apply TWICE a day when required	15/02

Close Print Letters

Once you have reviewed each control patient on the list to determine their eligibility, you are ready to print the letters and surveys.

Step 10. Mail pack to each included control patient

On the screen showing the list of patients, select **Show Control Patients** and click on the **Print Letters** button. Please enter your name when prompted. This will print the materials for each control patient that you have not excluded.

Collate the printed material as follows:

- The first page is a personalised letter to the patient explaining that the pharmacy is participating in the research project. Please sign the bottom of this letter. This letter is to be placed in an A4 envelope. This envelope will already contain an educational brochure about asthma ('Asthma: the basic facts').
- All documents with a small 'A' in the bottom right hand corner are to be placed in 'Envelope A – Information for your doctor'. There should be a letter to the GP and an 'Evaluation by General Practitioners' survey. This envelope will already contain a General Practitioner Project Information Sheet and a reply paid envelope for the GPs to return their completed survey in.
- All documents with a small 'B' in the bottom right hand corner are to be placed in 'Envelope B – Please join our survey'. There will be three patient surveys titled 'Patient Asthma Survey (Quality of Life)', 'Patient Asthma Survey (Asthma Control)', and 'Patient Asthma Survey (Medication Adherence)'. Envelope B will already contain a Survey Information Sheet and a reply paid envelope for the patients to return their completed surveys in.
- Place envelope A and envelope B inside the A4 envelope.

Address labels for the A4 envelopes can be printed by placing Avery L7162 label sheets in the A4 paper tray of your notes printer. Select **Print Labels**.

Alternatively, address labels for the A4 envelopes can be printed using Fred.

Send the packs to all included intervention patients with \$1.00 postage.

At this point you will given instructions on how to claim your final payment, which will include reimbursement for postage costs.

You have now finished the project.

Thankyou for your participation!

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Appendix 17. Patient intervention letter

<patient name>	<proprietor name>
<patient address>	<pharmacy name>
<patient suburb>	<pharmacy address>
<patient state> <postcode>	<pharmacy suburb>
	<pharmacy state> < postcode>
	Ph: <ph num> fax: <fax num>

Improving the control of asthma

<date>

Dear <patient name>

Our pharmacy is taking part in a research project with the University of Tasmania's School of Pharmacy to try and improve the control of asthma in the community.

I have enclosed some information about asthma, because I noticed that you have had 6 or more asthma reliever medications dispensed from the pharmacy in the last year. This may be a sign that your asthma control could be improved.

Just to make sure that your asthma is under control and that you are getting the best possible treatment, I suggest that you please do both of the following:

1. Help us help you - make an appointment with your GP

Please take **Envelope A- INFORMATION FOR YOUR DOCTOR** along to this appointment. This includes a letter for the doctor and your prescription dispensing record which will help the doctor assess your asthma control.

AND

2. Help us help others - join our survey

Please read the information inside **Envelope B - PLEASE JOIN OUR SURVEY**. Complete the surveys and return them to the University in the supplied reply paid envelope. This will help us develop a better understanding of asthma and how it affects people in the community.

Please be assured that your identity has not been released to the University, and the survey forms are all anonymous.

If you have any questions about this project, or your asthma, please give me a call at the pharmacy.

Yours Sincerely

<pharmacist name>

Appendix 18. Patient asthma control survey

Patient Asthma Survey (Asthma Control)

Please complete *all* questions by ticking the box that best describes how you have been during the *last two weeks as a result of your asthma*.

		All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	During the last 2 weeks, how much of the time did your asthma keep you from getting as much done at work, school or home?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
		More than once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all
2	During the last 2 weeks, how often have you had shortness of breath?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
		4 or more nights a week	2 or 3 nights a week	Once a week	Once or twice	Not at all
3	During the last 2 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness) wake you up at night or earlier than usual in the morning?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
		3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all
4	During the last 2 weeks, how often have you used your rescue inhaler or nebuliser medication?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
		Not at all controlled	Poorly controlled	Somewhat controlled	Well controlled	Completely controlled
5	How would you rate your asthma control during the last 2 weeks?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6	What is your age?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
		< 18	18-29	30-39	40-49	50-59
						60+
7	What is your gender		Male	Female		
			<input type="checkbox"/>	<input type="checkbox"/>		
8	Do you have a written Asthma Action Plan, that is, written instructions of what to do if your asthma is worse or out of control?		Yes	No		
			<input type="checkbox"/>	<input type="checkbox"/>		

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<Patient ID>

B

Appendix 19. Patient quality of life survey

Patient Asthma Survey (Quality of Life)

Please complete *all* questions by ticking the box that best describes how you have been during the *last 2 weeks as a result of your asthma*.

In general, how much of the time during the last 2 weeks did you:	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time
1 Feel short of breath as a result of your asthma?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2 Feel bothered by or have to avoid dust in the environment?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 Feel frustrated as a result of your asthma?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4 Feel bothered by coughing?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5 Feel afraid of not having your asthma medication available?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6 Experience a feeling of chest tightness or chest heaviness?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7 Feel bothered by or have to avoid cigarette smoke in the environment?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8 Have difficulty getting a good night's sleep as a result of your asthma?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9 Feel concerned about having asthma?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10 Experience a wheeze in your chest?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11 Feel bothered by or have to avoid going outside because of weather or air pollution?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

How limited have you been during the last 2 weeks doing these activity as a result of your asthma?

	Totally limited	Extremely limited	Very limited	Moderate limitation	Some limitation	A little limitation	Not at all limited
12 Strenuous activities (such as hurrying, exercising, running up stairs, sports)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13 Moderate activities (such as walking, housework, gardening, shopping, climbing stairs)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14 Social activities (such as talking, playing with pets/children, visiting friends/relatives)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15 Work related at activities* (tasks you have to do at work)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**If you are not employed or self-employed, these should be tasks you have to do most days*

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

<Patient ID>

B

Appendix 20. Patient medication adherence survey

Patient Asthma Survey (Medication Adherence)

Many people find a way of using their medicines that suits them. This may differ from the instructions on the label or from what their doctor had said. Here are some ways in which people have said they use their asthma medications. For each statement, please tick the box that best applies to you.

	Never	Rarely	Sometimes	Often	Always
1 I get confused about my asthma medications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2 I have strict routines for using my regular asthma medications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 I keep my asthma medications close to where I need to use them	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4 I ensure I have enough asthma medications so that I don't run out	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5 I push myself to follow the instructions of my doctors	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6 I make changes in the recommended asthma management to suit my lifestyle	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7 I vary my recommended asthma management based on how I am feeling	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8 I put up with my asthma symptoms before taking any action	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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<Patient ID>

B

Appendix 21. Patient survey information sheet

Improving the control of asthma

SURVEY INFORMATION SHEET

Why this research is needed

Asthma affects over 2 million Australians and causes thousands of hospital admissions each year. Recent findings suggest that the control of Asthma in Australia needs to be improved.

Aim of this research

The aim of this research is to improve the control of asthma and develop a better understanding of asthma and how it affects people in the community.

About the survey

The survey is being conducted by the University of Tasmania's School of Pharmacy with the help of selected pharmacies in Tasmania.

Special note on privacy

Please be assured that your identity has not been released to the University. No one at the University can identify the information that you provide; your survey forms are anonymous.

How can you help?**All you have to do is:**

1. Complete the three surveys the best you can;
2. Use the enclosed reply paid envelope to post them to the University.

What next?

In about 12 months, your pharmacist will send you another survey, to see how helpful the information was.

Any problems?

If you have any concerns or queries about the survey or your participation in the project, please contact your regular pharmacist, or Bonnie Bereznicki at the Tasmanian School of Pharmacy on telephone 6226 2191 or email bonnie.bereznicki@utas.edu.au.

The project has received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee. If you have any concerns of an ethical nature or complaints about the manner in which the project is conducted, you may contact the Executive Officer of the Tasmanian Human Research Ethics Committee (Tasmania) Network on 62267479 or human.ethics@utas.edu.au. You will need to quote ethics reference number H9823.

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia



Appendix 22. GP letter

<proprietor name>
<pharmacy name>
<pharmacy address>
<pharmacy suburb>
<pharmacy state> <postcode>
Ph: <ph num> fax: <fax num>

Improving the control of asthma

Dear Doctor

<Pharmacy Name> is participating in a research project with the University of Tasmania's School of Pharmacy which aims to identify patients whose asthma may not be optimally controlled and refer these patients to their GP for a review of their asthma therapy.

One of your patients, <Patient Name>, has been identified by <Pharmacy Name> as possibly requiring a review of <his/her> asthma therapy. That is, as evidenced by the accompanying prescription dispensing information, your patient has received six (6) or more reliever medications in the last 12 months. This usage, if reflecting dispensing, would exceed 3 puffs of reliever medication per day, which is clearly higher than that recommended by the National Asthma Council and the Asthma Foundation as indicating good control.

The prescription dispensing record from the pharmacy indicates that <Patient Name> has had <collated relievers and preventers> in the last 12 months. A full dispensing history appears below.

No. Dispensings <number>	Last Dispensed <date>	Drug Name <drug name and dose>
-----------------------------	--------------------------	-----------------------------------

<Patient Name> has been provided with educational material regarding asthma and has been asked to contact <his/her> GP for a review of <his/her> asthma. This may be an opportunity for you to develop or review the patient's written Asthma Action Plan.

I kindly ask that you complete the attached GP survey regarding your perceptions of this program.

Please see the enclosed Project Information Sheet for more information regarding the project. If you would like further information about any aspect of the project, please contact me at the pharmacy, or Bonnie Bereznicki at the Tasmanian School of Pharmacy on telephone: 6226 2191 or email: bonnie.bereznicki@utas.edu.au.

Thankyou for your assistance.

Yours Sincerely

<Pharmacist name>

Appendix 23. GP survey

Improving the control of asthma

EVALUATION BY GENERAL PRACTITIONERS

Please complete this survey at the end of the consultation and post using the reply paid envelope provided.

Date of Consultation: / /

1. I modified (or intend to modify) my patient's therapy as a result of the pharmacist's referral				
Yes	<input type="checkbox"/>	Please elaborate...	<div style="border: 1px solid black; height: 20px; width: 100%;"></div> <div style="border: 1px solid black; height: 20px; width: 100%;"></div>	
No	<input type="checkbox"/>			
2. I feel that the pharmacist appropriately identified my patient as needing a review of their asthma therapy				
Yes	<input type="checkbox"/>	If No, what is the reason?	<div style="border: 1px solid black; height: 20px; width: 100%;"></div> <div style="border: 1px solid black; height: 20px; width: 100%;"></div>	
No	<input type="checkbox"/>			
3. I believe that my patient will benefit from this intervention				
<input type="checkbox"/> Strongly agree	<input type="checkbox"/> Agree	<input type="checkbox"/> Neutral	<input type="checkbox"/> Disagree	<input type="checkbox"/> Strongly disagree
4. I believe that pharmacists, utilising dispensing records, are well placed to identify patients who may need review of their asthma by their doctor				
<input type="checkbox"/> Strongly agree	<input type="checkbox"/> Agree	<input type="checkbox"/> Neutral	<input type="checkbox"/> Disagree	<input type="checkbox"/> Strongly disagree
5. I believe that there is an evident need for improved asthma control in the community				
<input type="checkbox"/> Strongly agree	<input type="checkbox"/> Agree	<input type="checkbox"/> Neutral	<input type="checkbox"/> Disagree	<input type="checkbox"/> Strongly disagree
6. I believe that this type of program delivered by community pharmacists would be likely to improve asthma control in the community, if implemented on a larger scale				
<input type="checkbox"/> Strongly agree	<input type="checkbox"/> Agree	<input type="checkbox"/> Neutral	<input type="checkbox"/> Disagree	<input type="checkbox"/> Strongly disagree
7. Do you have any general or specific comments regarding this intervention program?				
<div style="border: 1px solid black; height: 40px; width: 100%;"></div>				

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

<Patient ID>

A

Appendix 24. Pharmacist satisfaction survey

Improving the control of asthma

PHARMACIST SATISFACTION SURVEY

Thank you for participating in this project. Please complete this survey at the end of the six-week intervention period. Your input is valued and greatly appreciated.

1. I believe that there is an evident need for improved asthma control in the community
☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree
2. I believe that this project appropriately identified patients with poorly controlled asthma
☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree
3. I believe that the patients identified to be in the intervention group will generally benefit from this project
☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree
4. I believe that mailing information and surveys to patients only is an appropriate way to help them improve their asthma management and control
☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree
5. I believe that handing out information and surveys to patients (face-to-face) only is an appropriate way to help them improve their asthma management and control
☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree
6. Which type of intervention would you prefer to perform in usual practice?
☐ Mailed ☐ Face-to-face

Please elaborate

.....
.....
.....
.....
.....

1 of 3

7. The education session for pharmacists increased my confidence in dealing with asthma management issues

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree ☐ Did not attend

8. The education session for pharmacists increased my confidence in using the MedeMine program

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree ☐ Did not attend

9. I found the MedeMine program simple to use

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

10. Participation in this project required a minimal amount of my time

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

How much time would you estimate that you needed to spend for **each** patient?.....

11. Using the MedeMine program and implementing the intervention negatively impacted my usual workflow

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

12. I believe that the potential benefits to patients with asthma outweighed the impact on my workflow

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

13. I would feel more confident about managing patients with asthma if MedeMine was routinely available to use

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

14. I believe that pharmacists, utilising dispensing records, are well placed to identify patients who may need review of their asthma by their doctor

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

15. I believe that this type of program delivered by community pharmacists will improve asthma control in the community if implemented on a larger scale

☐ ☐ ☐ ☐ ☐
Strongly agree Agree Neutral Disagree Strongly disagree

16. Did you receive any feedback (positive or negative) from patients or GPs regarding this project?

☐ ☐
Yes No

If yes, please elaborate

.....
.....
.....
.....
.....

17. Do you have any general or specific comments or concerns regarding this project?

.....
.....
.....
.....
.....

18. Would you be willing to participate in other similar projects utilising dispensing records to improve the management of chronic diseases?

☐ ☐ ☐
Yes No Unsure

----- END OF SURVEY -----

Thank you for completing this survey

Please either hand back to your Project Officer
or post to the University using the reply paid envelope provided

This program is funded by the Australian Government Department of Health and Ageing as
part of the Fourth Community Pharmacy Agreement through the Fourth Community
Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

3 of 3

Appendix 25. Patient satisfaction survey

Patient Satisfaction Survey

Please complete all questions by filling in the box with a mark that best describes your opinions about this project.

	Strongly agree	Agree	Unsure	Disagree	Strongly disagree
1 I feel that I was appropriately identified by my pharmacist as needing a review of my asthma by my doctor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2 Use of my asthma reliever medication (Ventolin, Airomir, Asmol, Bricanyl) has reduced over the last year	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 I found the information on asthma management that was sent out with the surveys 12 months ago useful	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4 I believe that my asthma control has improved as a result of this project	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5 I believe that pharmacists are well placed to identify patients who may need a review of their asthma by their doctors	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6 I believe that this type of program delivered by community pharmacists will improve asthma care in the community if implemented in a larger program	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7 I am satisfied with the level of asthma care that I usually receive from my doctor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8 I am satisfied with the level of asthma care that I usually receive from my pharmacist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9 I regularly discuss my asthma control and/or management with my pharmacist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10 Do you have any general or specific comments or concerns regarding this project?	<div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div> <div style="border-bottom: 1px dotted black; height: 10px; margin-bottom: 2px;"></div>				

This program is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

<Patient ID>

B

Appendix 26. Intervention follow-up instructions for researchers

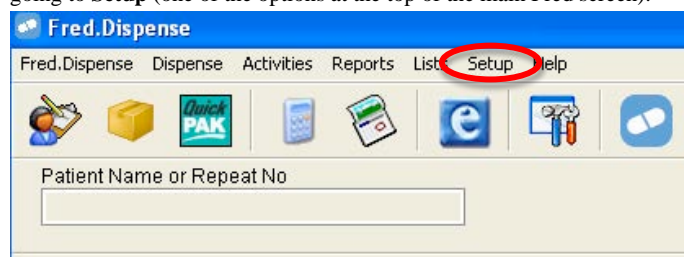
Pharmacy dispensing records to identify and educate patients with suboptimal asthma management

Intervention follow-up instructions for researchers

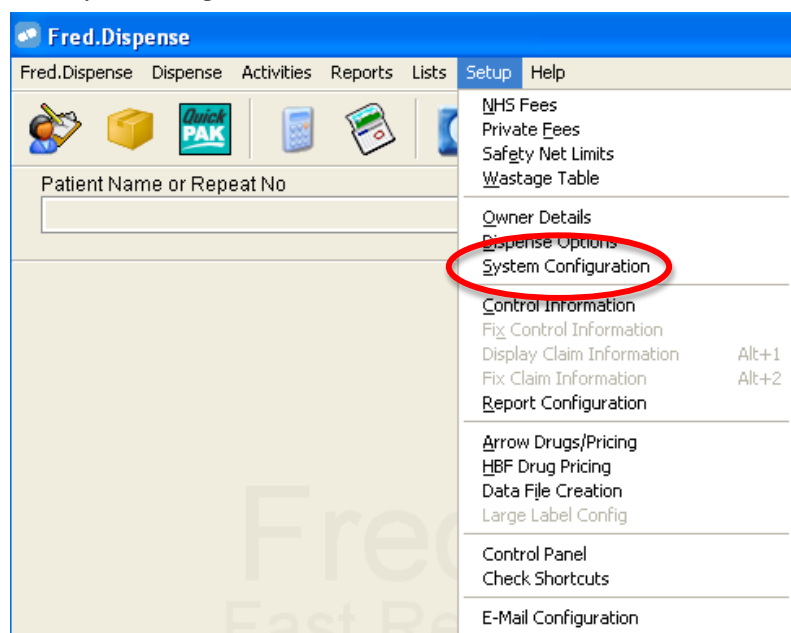
Step 1. Locate Fred Server

The MedeMine program should be located on the Fred Server computer.

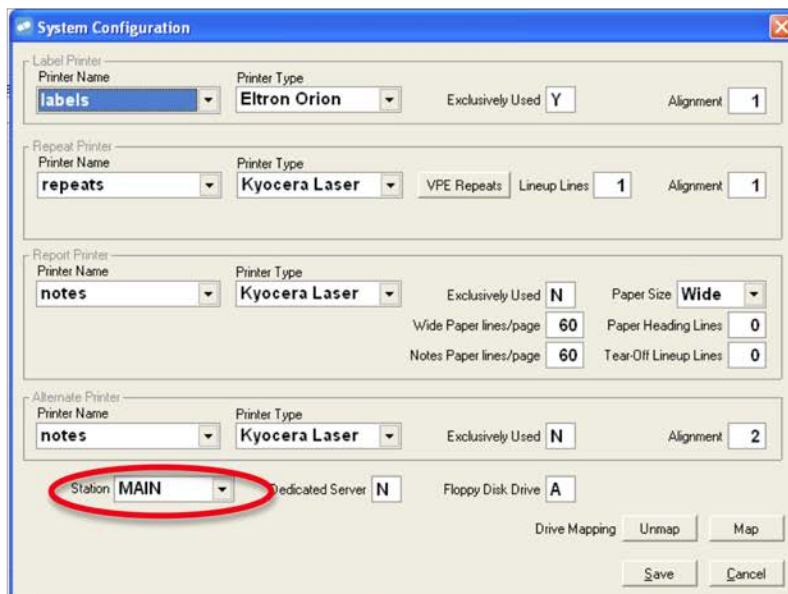
If the pharmacist is not sure which computer is the Fred Server, you can check in Fred, by going to **Setup** (one of the options at the top of the main Fred screen):



Select **System Configuration**:

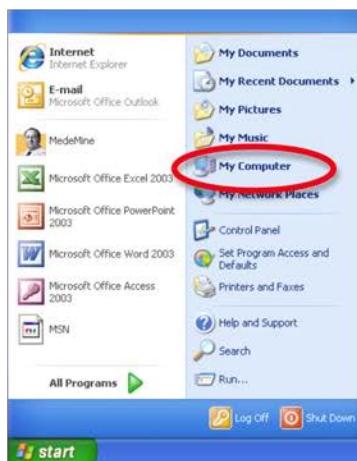


If you are using the Fred Server, the **Station** will be **MAIN**, if you are not at the Fred Server, the **Station** will be **TERMINAL**:



Step 2. Locate the MedeMine program*

You need to locate and update the MedeMine program on the Fred Server. It should be located in **Program Files** on the **C-drive**. Go to **My Computer** and open the **C-drive**:



In the C-drive, locate and double-click on **Program Files**, then locate and double click on the **MedeMine** folder. The **MedeMine** Icon should be located in this folder.



NB: Do not open the MedeMine program yet; it needs to be updated first.

*If the MedeMine program has been wiped, refer to Appendix 1 for further instructions.

Step 3. Update the MedeMine program

Insert your USB device into the server's USB drive. Copy the updated version of **MedeMine** and from your USB device and paste it into the **MedeMine** folder on the server.

You will be asked if you want to replace the existing file. Click **Yes**.

NB: If the Server does not have a working USB drive, you can download the updated version of MedeMine from:

<http://www.pharmacy.utas.edu.au/UMORE/downloads/medemine.exe.zip>

Step 4. Run the MedeMine program

1. Double-click on the new MedeMine icon [My Computer - Local Disk (C:) - Program Files - MedeMine folder - MedeMine icon].



You will see the first screen:

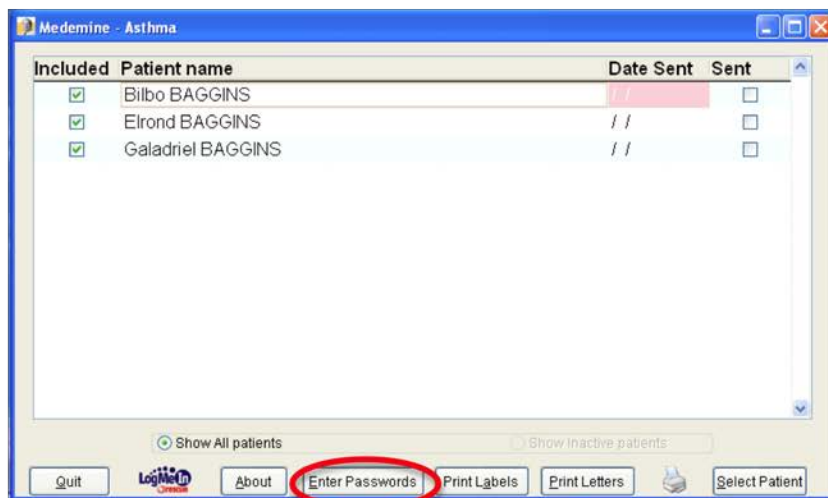


Make sure the Program Version is correct (2.1.30)

If the version is different, follow Step 3 again.

*If you missed checking the version on this screen (it may only appear for an instant), you can check it by clicking **About** on the main screen (below).*

After a brief pause you will see the main window:



3

Left-click on the **Enter passwords** button (see previous figure) and enter the password:

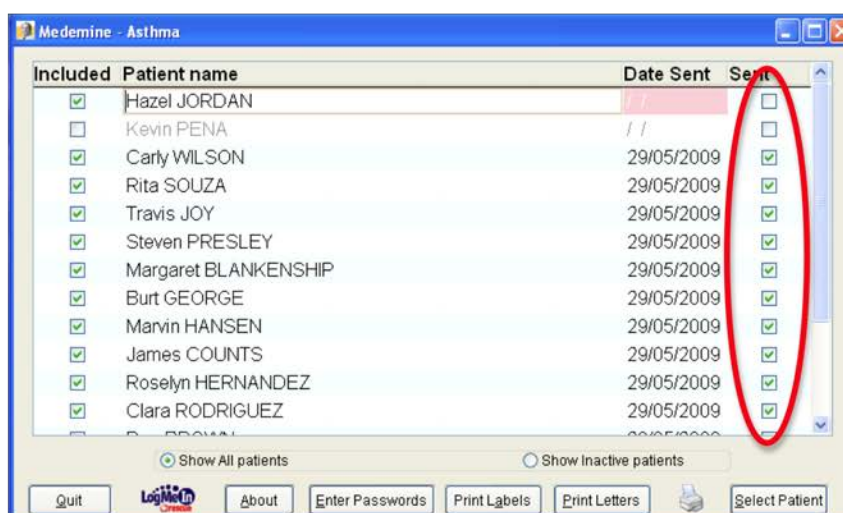
A57MaD3m [A(five)(seven)MaD(three)m]

After you have entered the correct password, the program will pause for a moment (while it transfers some files) and you can continue (if you enter the password incorrectly, the screen will “shake”).

Step 5. Exclude any intervention patients who DIDN'T receive an intervention

Because we are sending follow-up letters to the intervention patients, we need to exclude any INCLUDED patients who did not receive an intervention, to ensure they are not sent follow-up letters.

When the pharmacists printed the intervention letters last year, a tick would have been placed in the “sent” column:



If the patient met the inclusion criteria, but did NOT receive an intervention, the “included column” would have been ticked, but the “sent” column would NOT be ticked

See the first patient in the above figure - you need to exclude this patient (the second patient has ALREADY been excluded [neither column ticked, plus name in faded text], and all other patients received the intervention [both columns ticked]).

To exclude a patient for this reason:

Double left-click on the patient’s name.

This will open up an individual patient’s file.

Viewing Asthma trial for Mrs Hazel JORDAN

MRS Hazel JORDAN
24 McLachlan Street
Connangorach 3401

Reason for Exclusion [Dropdown]

Initial Letter Printed on: [Date/Time] **Second Letter Printed on:** [Date/Time] **Seen by GP** [Checkbox]

Months History to display [Radio buttons: 1, 3, 6, 9, 12, All]

Disp	Drug Name	Qty	Directions	Doc	Rpt	Dp	\$	By
21/04	VENTOLIN CFC FREE	2	Shake well and inhale	CHH	5	6	6.50	KO
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				376416	
08/04	VENTOLIN CFC FREE	2	Shake well and inhale	KND	5	5	6.50	KF
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				374978	
24/03	VENTOLIN CFC FREE	2	Shake well and inhale	CHH	5	5	6.50	KO
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				372981	
11/03	VENTOLIN CFC FREE	2	Shake well and inhale	KND	5	4	6.50	KP
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				371232	
20/02	VENTOLIN CFC FREE	2	Shake well and inhale	CHH	5	4	6.50	GP
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				368894	
28/01	VENTOLIN CFC FREE	2	Shake well and inhale	KND	5	3	6.50	KP
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				365941	
21/01	VENTOLIN CFC FREE	2	Shake well and inhale	KND	5	6	6.50	KP
2009	MET-AERO 200 Dose		ONE to TWO puffs by mout				365064	

Close **Print Letters**

To EXCLUDE this patient, select the **Reason for Exclusion** drop-down menu - this is located in the top right-hand corner of the screen.

Viewing Asthma trial for Bilbo BAGGINS

Bilbo BAGGINS

Reason for Exclusion [Dropdown]

- Too confused
- Deceased
- Patient has COPD
- Nursing Home Resident
- May cause undue distress
- Under 19 years old
- Other**
- Letter returned to sender
- Declines to participate
- Prefers no further contact
- Privacy concerns
- Other ...

31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every				8877	
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU				8874	
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	50mcg 60d		mouth TWICE a day **REGU				8876	
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-AERO 200 Dose		TWO puffs by mouth every				8873	

Close **Print Letters**

Select **Other....** and type the type **NIG** (short for “no intervention given”) and your initials.

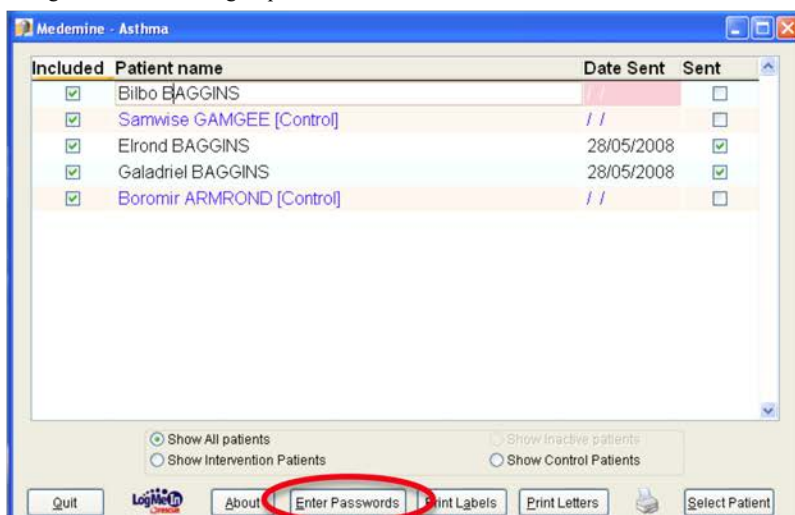
Once you have typed a reason for exclusion, you will be directed to the **Extra Information** screen. Click **Close**. This will take you back to the list of patients.

Step 6. Enter the follow-up phase password

Left-click on the **Enter passwords** button and enter the password:

3nd1t [(three)nd(one)t]

After you have entered the correct password, the program will reveal the names of the patients assigned to the control group:



Step 7. Select printer

Before printing anything, you need to check that the printer is set up correctly. The program should have automatically selected the printer that you normally print notes or CMIs to.

To check if the program has selected the correct printer; click on the picture of the printer as shown on the right (located on the bottom right-hand side of the screen showing the list of patients)



Select the printer that normally prints A4 pages from Fred.

Ensure there is enough paper in the printer.

Step 8. Print follow-up letter and surveys for included intervention patients

In the following order,

1. On the main screen, select **Show Intervention Patients**
 - This will give you a list of all intervention patients who were originally sent a pack and not subsequently excluded from the trial.
2. Select **Print Letters**
 - Please enter the pharmacist's name when prompted. The program will print four surveys and a cover letter for each intervention patient who was originally sent a pack and not subsequently excluded from the trial.

The first page is a personalised letter to the patient. Please ask the pharmacist to sign the bottom of this letter.

There will be four patient surveys titled 'Patient Asthma Survey (Quality of Life)', 'Patient Asthma Survey (Asthma Control)', 'Patient Asthma Survey (Medication Adherence)' and 'Patient Satisfaction Survey'.

Place each letter with its surveys in the blank C5 envelope. This envelope should already contain a reply paid envelope for the patients to return their completed anonymous surveys to the University, and a Survey Information Sheet.

PLEASE DO NOT SEPARATE THE COVER LETTER FROM ITS MATCHING SURVEYS. THE SURVEYS ARE UNIQUELY CODED TO MATCH THE PATIENT.

Address labels for the C5 envelopes can be printed by placing Avery L7162 label sheets face-down in the A4 paper tray of the notes printer the A4 paper tray of the notes printer. Select **Print Labels**.

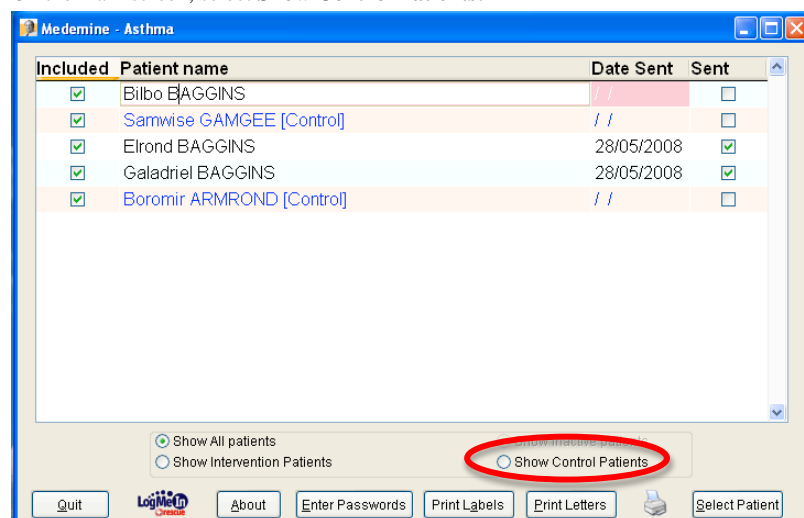
Alternatively, address labels for the C5 envelopes can be printed using Fred.

Double check that postcodes have been included on the address labels. Add if necessary.

Mail the letters and surveys to all included intervention patients with \$1.10 postage.

Step 9. Exclude any control who no longer qualify for an intervention

On the main screen, select **Show Control Patients**:



This will give you a list of patients who were originally identified as receiving 6 or more canisters of asthma reliever medication (salbutamol/terbutaline) the 12 months prior to the project start date, and who were assigned to the control group.

You now need to exclude any of the control patients who meet the pre-defined exclusion criteria.

Double left-click on the control patient's name.

Viewing Asthma trial for Bilbo BAGGINS

Bilbo BAGGINS
An Address
A Suburb 7000

Reason for Exclusion

Initial Letter Printed on: / / : : AM
Second Letter Printed on: / / : : AM
Seen by GP ☐

Months History to display ☐ 1 ☐ 3 ☐ 6 ☐ 9 ☒ 12 ☐ All

Disp	Drug Name	Qty	Directions	Doc	Rpt	Dp	\$	By
23/04	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	3	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8883
27/03	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	2	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8881
28/02	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	1	6.50	NB
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8879
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU					8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	50mcg 60d		mouth TWICE a day **REGU					8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-AERO 200 Dose		TWO puffs by mouth every					8873
22/11	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	4	6.40	DC

Close Print Letters

This will open up an individual patient's file as seen:

All included control patients will be sent an intervention pack. Therefore, you will need to exclude any control patients who no longer qualify for an intervention pack, that is, if they have received less than 6 canisters of asthma reliever medication in the past 12 months.

Select a patient, click on **Collated History** and select **12** months:

Viewing Asthma trial for Samwise GAMGEE

Samwise GAMGEE
Bag End
The Shire 7000

Reason for Exclusion

Initial Letter Printed on: / / : : AM
Second Letter Printed on: / / : : AM
Seen by GP ☐

Months History to display ☐ 1 ☐ 3 ☐ 6 ☒ 12 ☐ All

Collated History

#	DISP	Drug name	Directions	last Disp
11	Celecoxib CAP 200mg (30)	Take ONE capsule daily immediately after food	22/04 2008	
11	Sformoterol T-HALER 6mcg (1)	Inhale ONE dose by mouth TWICE a day as directed by your doctor	22/04 2008	
11	Fluticasone A-HALER 250mcg (1)	Inhale ONE dose by mouth TWICE a day *Rinse mouth out with water after use	22/04 2008	
11	Roxithromycin TAB 300mg (5)	Take ONE tablet with a glass of water daily about 15 mins before food until fin	26/04 2008	
10	Salbutamol Cfc Free MET-AERO 200 Dose (2)	Shake well and inhale TWO puffs by mouth every FOUR hours when required	22/04 2008	
9	Codeine & Paracetamol TAB 500-	Take HALF a tablet FOUR times a day when required as directed	22/04 2008	
9	Ranitidine TAB 150mg (60)	Take ONE tablet TWICE a day	22/04 2008	
7	Paracetamol TAB	Take TWO tablets every FOUR hours when	22/04	

Close Print Letters

Exclude any control patients who have received less than 6 relievers (Salbutamol, Ventolin, Asmol, Airomir, Terbutaline, Bricanyl) in the last 12 months.

NB: Most relievers are dispensed in supplies of two canisters. The number on the left of the drug name is the number of dispensings, not the quantity of canisters. In the previous figure, there were 10 dispensings of salbutamol (2) – note the quantity of canisters in brackets after the drug name. Therefore the total number of supplies was 20 canisters in 12 months.

Date	Drug Name	Quantity	Instructions	STOA	5	6	Cost	DC
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU					8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	50mcg 60d		mouth TWICE a day **REGU					8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-AERO 200 Dose		TWO puffs by mouth every					8873

To exclude such patients from receiving an intervention pack, select **Other....** from the drop-down **Reason for Exclusion** menu and type **NIR** (short for “no intervention required” and your initials).

You will be directed to the **Extra Information** screen, just click **Close**.

Step10. Exclude any control patients who meet the exclusion criteria

For each control patient identified by the software, you will also need to exclude any who meet the pre-defined exclusion criteria, listed in the drop-down **Reason for Exclusion** menu, ABOVE the black line:

Date	Drug Name	Quantity	Instructions	STOA	5	6	Cost	DC
31/01	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	6	6.50	DC
2008	MET-AERO 200 Dose		TWO puffs by mouth every					8877
31/12	FLIXOTIDE A-HALER	1	Inhale ONE dose by	STOA	1	1	4.90	DC
2007	500mcg		mouth TWICE a day **REGU					8874
31/12	SEREVENT A-HALER	1	Inhale ONE dose by	STOA	5	1	4.90	DC
2007	50mcg 60d		mouth TWICE a day **REGU					8876
24/12	VENTOLIN CFC FREE	2	Shake well and inhale	STOA	5	5	6.40	DC
2007	MET-AERO 200 Dose		TWO puffs by mouth every					8873

- Too confused
- Deceased
- Patient has COPD
- Nursing home resident
- May cause undue distress
- Under 18 years old
- If you have another reason to exclude the patient select **other....** and type the reason.

You will need the pharmacist's input to determine whether the patients meet any of these criteria (this process was completed for the intervention patients last year).

Once you have selected a reason for exclusion for a patient, you will be directed to the **Extra Information** screen. If you have any information to add as to why the patient should be excluded, you can free-type in the boxes within this screen. Otherwise, just click **Close**. This will take you back to the list of patients.

Once you have reviewed each control patient on the list to determine their eligibility, you are ready to print the control patients' letters and surveys.

Step 11. Print letters and surveys for included control patients

On the screen showing the list of patients, select **Show Control Patients** and click on the **Print Letters** button. Please enter the pharmacist's name when prompted. This will print the materials for each control patient that you have not excluded.

PLEASE DO NOT SEPARATE THE COVER LETTER FROM ITS MATCHING SURVEYS. THE SURVEYS ARE UNIQUELY CODED TO MATCH THE PATIENT.

Collate the printed material as follows:

- The first page is a personalised letter to the patient explaining that the pharmacy is participating in the research project. Please ask the pharmacist to sign the bottom of this letter. This letter is to be placed in the blank A4 envelope. This envelope should already contain an educational brochure about asthma ('Asthma: the basic facts').
- All documents with a small **A** in the bottom right hand corner are to be placed in **Envelope A – Information for your doctor**. There should be a letter to the GP (one or two pages) and an 'Evaluation by General Practitioners' survey. This envelope should already contain a reply paid envelope for the GPs to return their completed anonymous surveys to the University, and a General Practitioner Project Information Sheet. Please ask the pharmacist to sign the end of the GP letter.
- All documents with a small **B** in the bottom right hand corner are to be placed in **Envelope B – Please join our survey**. There will be three patient surveys titled 'Patient Asthma Survey (Quality of Life)', 'Patient Asthma Survey (Asthma Control)', and 'Patient Asthma Survey (Medication Adherence)'. Envelope B should already contain a reply paid envelope for the patients to return their completed anonymous surveys to the University, and a Survey Information Sheet.
- Leave Envelopes A and B unsealed, and place them inside the A4 envelope.

Address labels for the A4 envelopes can be printed by placing Avery L7162 label sheets face-down in the A4 paper tray of the notes printer. Select **Print Labels**.

Alternatively, address labels for the A4 envelopes can be printed using Fred.

Double check that postcodes have been included on the address labels. Add if necessary.

Send the packs to all included control patients with \$1.10 postage.

Step 12. Print payment instructions

The pharmacist is now eligible to claim for their final payment.

Please ascertain whether or not the pharmacists will be posting the envelope themselves (and therefore will need to be reimbursed for postage costs).

In the MedeMine program, you need to type ONE of the following passwords:

payme\$ [payme(shift four)] if THE PHARMACIST is mailing the packs

or

cH33p5k8 [cH(three)(three)p(five)k(eight)] if YOU are mailing the packs

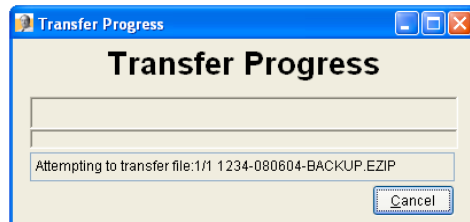
This will print instructions for the pharmacist on how to claim their payment.

NB: The amount should be \$100.00 ± \$1.10 per pack mailed. The date the invoice is due will also be worked out automatically, as six weeks from the date the instructions are printed.

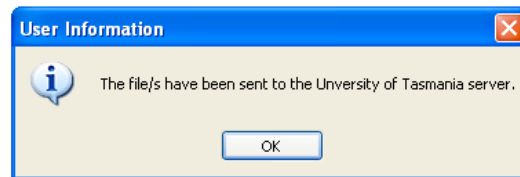
Step 13. Close the MedeMine program

You can now close the MedeMine program.

When the MedeMine program closes, this screen will appear:



When this is complete, this screen will appear.



Step 14. Obtain a back-up of the de-identified dispensing data

Create a new folder on your USB device, and name it with the pharmacy's approval number.

Go to **My Computer** and open the **C-drive**.

Locate and double-click on **Program Files**. Locate and double click on the **MedeMine** folder.

In the MedeMine folder, locate the **Data** folder and the **Backups** folder.

Copy both the **Data AND Backups** folder to the folder you created on your USB device.

Eject your USB device.

Step 15. Update the MedeMine shortcut on the desktop

Most pharmacies will have a MedeMine shortcut located in a MedeMine folder on the desktop. This shortcut will no longer work once you have updated the program.

To update this shortcut, right-click on the **MedeMine** icon inside the MedeMine folder located in Program Files and select "**Create Shortcut**". Copy this shortcut to the MedeMine Folder on the desktop and delete the old MedeMine icon inside this folder.

Appendix 1. If MedeMine program has been wiped from the Fred Server

NB: You need to be 100% sure that the program has been wiped before doing this (do a search for “MedeMine”).

If you’re not sure, please call Bonnie on 03 6226 2191 or 0407 550 115.

2. Locate the backup data belonging to the pharmacy on your USB device. It will be a folder named according to the pharmacy’s name and/or approval number.
3. Copy this folder onto the **C-drive** [My Computer - Local Disk (C:)] on the Fred Server. Double check that you have copied the correct data over.
4. Rename the data folder that you have just pasted, as **Data**.
5. Locate the installation package on your USB device. It is called **MedeMinev2.1.26.exe**. Copy it to the Server’s desktop.
6. Double-click on the installation package, and follow the prompts by clicking “next” etc. until the installation is complete.
7. If the installer package created a MedeMine shortcut on the desktop, you can delete it – it is the old version and needs to be updated.
8. Locate the updated MedeMine program on your USB device. It is called **Medemine.exe**. Copy the program and paste it in the **MedeMine** folder inside **Program Files**. [My Computer - Local Disk (C:) - Program Files - MedeMine].
9. Go to Step 4: Run the MedeMine program.

Appendix 2. MedeMine passwords

Password	Description
A57MaD3m	Asthma denominators. Historical use of denominators if program was run in all the years the dispensing package recorded info.
3nd1t	Used to 'end the trial' – sets the finished flag to true, and enters the stop date of the trial.
payme\$	Displays the contact details and the amount the pharmacist can send an invoice (postage included).
cH33p5k8	Displays the contact details and the amount the pharmacist can send an invoice, where only the base price and not postage is calculated.

Appendix 27. Follow-up patient letter

<patient name>
<patient address>
<patient suburb>
<patient state> <postcode>

<proprietor name>
<pharmacy name>
<pharmacy address>
<pharmacy suburb>
<pharmacy state> <postcode>
Ph: <ph num> fax: <fax num>

Improving the control of asthma

<date>

Dear <patient name>

<Pharmacy name> is taking part in a research project with the University of Tasmania's School of Pharmacy to try and improve the control of asthma in the community. You may recall that approximately 12 months ago we gave you some information about asthma and suggested that you visit your GP to discuss your asthma control.

We hope that the information was useful and that you have had success with the control of your asthma.

You may also recall that there were three surveys included in the information supplied to you. Although you may have already completed the surveys 12 months ago, we are hoping that you will fill out the short surveys again, to help my colleagues and I with our ongoing efforts to learn more about asthma, and see how people's asthma has changed over the last year.

All you have to do is:

1. Please complete the four surveys as best you can;
2. Used the enclosed reply paid envelope to post them to the University

Please be assured that your identity has not been released to the University, and the survey forms are all anonymous.

If you have any questions about this project, or your asthma, please give me a call at the pharmacy.

Yours Sincerely

<pharmacist name>

Appendix 28. Pharmacist invitation letter



Understanding patient experiences with respiratory medication

<Date>

Dear <Pharmacist Name>

As a healthcare provider in your local community you would be aware that one of the major contributing factors to both morbidity and mortality of patients with COPD is their non-adherence to drug therapy. With 20,000 cases of COPD diagnosed in Australia each year and with adherence to long-term preventive medication regimens being estimated to be as low as 28%, we are seeking your assistance.

The Tasmanian School of Pharmacy, in collaboration with P Group Research, is currently undertaking a research project aiming to identify and understand why patients are persistent or not with COPD therapy. The project will also form part of Bonnie Bereznicki's PhD thesis which aims to identify management issues relating to chronic respiratory conditions, and establish a potential new role for community pharmacists in this area.

In order to conduct this study, your involvement is vital for the patient recruitment process. A data mining software tool has been developed for the Fred dispensing system which enables easy identification of patients who may and may not be persisting with Spiriva® therapy. Should you wish to assist us with this important study, you will be asked to view the dispensing information for each identified respiratory patient and exclude any who meet the pre-specified exclusion criteria. The attached project synopsis highlights these criteria and is sensitive to individual patient situations. Demands on your time are minimal from this point as the software application will then automatically print invitation letters and consent forms for patients. Please note that no identifying information will be released to us unless the patient signs the consent form and returns it to the University.

The Tasmanian School of Pharmacy will then send the consenting patients a questionnaire assessing their health and illness beliefs and experiences with respiratory medication, and invite some patients to participate in qualitative face-to-face interviews with P Group researchers. Please refer to the attached project synopsis for further details on the proposed methodology.

We anticipate that participation in the study will require approximately 20 minutes of your time. Involvement in this project requires the use of the Fred dispensing system. If you would like to be involved or require further information about the project, please complete the attached form and fax back to the Tasmanian School of Pharmacy.

In order to thank you for your assistance with this study, we are offering \$500 to compensate you for your time and professional input.

The project has received ethical approval from the Tasmania Health and Medical Human Research Ethics Committee. If you have any concerns of an ethical nature or complaints about the manner in which the project is conducted, you may contact the Executive Officer of the

Tasmanian Human Research Ethics Committee (Tasmania) Network on 6226 7479 or human.ethics@utas.edu.au. You will need to quote ethics reference number H9842.

The project is being sponsored by Boehringer Ingelheim, and it is intended that the results will be disseminated to Australian GPs and pharmacists by presentations at national meetings and in peer-reviewed journals. We can assure you that no identifying information relating to patients, doctors or pharmacists will be disseminated. All project results will be de-identified and pooled.

Attached is a form for you to return to us if you are willing to participate in this project. Please either fax it back to us on 6226 7627 or send it back to us in the reply paid envelope provided.

If you have any queries regarding this project please contact Bonnie Bereznicki at the Tasmanian School of Pharmacy on 6226 2191. We will be contacting you shortly to discuss your willingness to participate in this project.

Yours sincerely,



Bonnie Bereznicki B.Pharm (Hons)
Clinical Research Pharmacist and PhD Candidate
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 83 Hobart
Tasmania 7001
Telephone 6226 2191
Facsimile 6226 7627
Bonnie.Bereznicki@utas.edu.au



Dr Shane Jackson B.Pharm (Hons) PhD MPS
Senior Research Fellow
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania



The research unit at the Tasmanian School of Pharmacy (UMORE; Unit for Medication Outcomes Research and Education) is a premier source of information, education and collaborative research in the assessment and improvement of medication outcomes.



P Group Research Pty Ltd specialised in delivering the highest quality in qualitative research and has available highly experienced consultants, all of which are AMSRS members and thus adhere stringently to the AMSRS Professional Code of Conduct and the Market and Social Research Privacy Principles. Their specialist interviewers have conducted hundreds of interviews with patients and are highly sensitive and empathetic to patient issues.

Appendix 29. Project synopsis for pharmacists



Understanding patient experiences with respiratory medication

Project Synopsis

The project objective is to understand the drivers and barriers of persistence with respiratory medication. The most effective and reliable method to accomplish this is to employ a key healthcare provider and resource - community pharmacists and their computerised prescription data. This will help identify patients with COPD as evidenced by their use of Spiriva® (tiotropium).

The research team has developed a software application that extracts data from the market leading pharmacy dispensing software system in Australia (Fred Dispense; PCA/NU Systems). The software application not only ensures correct identification of suitable participants, it also minimises the time required of the pharmacist. Community pharmacies throughout Tasmania will be invited to participate, and with their permission, a researcher will install the software application on the pharmacy dispensing computer.

The software will interrogate the dispensing history and produce a list of patients that meet the following criteria:

- “Persistent” patients: those to whom Spiriva® was dispensed at least nine times in the preceding 12-month period, including at least two units in the past 90 days.
- “Non-persistent” patients: those to whom Spiriva® was dispensed between one and four times (inclusive) in the preceding six-month period, with nil dispensings in the subsequent 65 days. Such patients would also have had nil Spiriva® dispensed in the 12-months prior to the first dispensing of Spiriva®.

The participating pharmacist will examine the dispensing information for each patient identified and will be able to exclude patients from being sent an invitation to participate if they believe the patient is aged under 40 years, is residing in an aged care facility, is deceased, is significantly cognitively impaired or would not understand the letter, or would be alarmed excessively by receiving the letter and participating in the project. Patients deemed suitable for inclusion will be sent a letter by the community pharmacist, to invite them to participate, along with patient information sheets and consent forms.

All consenting patients will subsequently be sent questionnaires by the researchers, assessing health and illness beliefs, experience with respiratory medication and general health-related demographic variables. Approximately half of the patients will also participate in qualitative face-to-face interviews addressing patient characteristics, diagnosis, treatment choice, day-to-day management, fulfilment, and persistence with therapy. Project deliverables will include utilising key dispensing information to identify key barriers and predictors of poor persistence to respiratory medication, and the development of belief/behaviour maps for identified patients, leading to a clear set of recommendations regarding persistence triggers amongst patient types.

All participating community pharmacists will be provided with the study’s key outcomes. It is intended that the outcomes of the study will improve awareness of the drivers and barriers of persistence with respiratory medication. Awareness of these drivers and barriers amongst patient types will make it easier for community pharmacists to offer targeted encouragement to patients to take their medication in the manner in which it was prescribed.

This project is funded by Boehringer Ingelheim

Appendix 31. Patient invitation letter

<patient name>
<patient address>
<patient suburb>

<proprietor name>
<pharmacy name>
<pharmacy address>
<pharmacy suburb>
Ph: <ph number>

Understanding patient experiences with respiratory medication

<date>

Dear <patient name>

Our pharmacy is taking part in a research project with the University of Tasmania to try to learn more about people's experiences with respiratory medication. The project is part of a pharmacy student's PhD thesis which aims to improve the management of chronic respiratory conditions.

What prompted me to write to you is that our records show that that you have received at least one supply of respiratory medication from the pharmacy over the past 12 months. The University is interested in learning about people's views and experiences, regardless of whether they are still taking respiratory medication or not.

Participation will involve filling out a questionnaire about your health, medical condition and respiratory medication use. You may also be asked if you would like to participate in a face-to-face interview.

The University is offering reasonable reimbursement to you for your participation in the project.

To participate in this project:

1. Read the information sheet and sign the consent form
2. Send the signed consent form to the University using the postage paid envelope provided, or fax it to 6226 7627 by Friday 18th April.

Your name and address will not be sent to the University unless you send them the signed consent form.

If you have any questions about this project, please give me a call at the pharmacy.

Thank you for your assistance.

Yours sincerely,

<pharmacist name>

This study has received financial support from Boehringer Ingelheim

Appendix 32. Patient consent form



Understanding patient experiences with respiratory medication

PATIENT CONSENT FORM

By signing this consent form I am agreeing to participate in this research project and declare that;

- 1 I have read and understood the 'Patient Information Sheet' for this research project. I acknowledge that the nature, purpose and contemplated effects of the project so far as it affects me, and I understand that my consent is given voluntarily.
- 2 I understand that the project involves the following procedures:
 - Upon signing the consent form and mailing it to the researchers, I will be sent a questionnaire regarding my health and medication use.
 - My pharmacy medication records and questionnaire results will be analysed by the researchers.
 - I may be asked to take part in a face-to-face interview about my experiences with respiratory medication.
- 3 Any questions that I have asked have been answered to my satisfaction.
- 4 I am informed that no information regarding any medical history will be divulged and the results of any questionnaires or interviews involving me will not be published so as to reveal my identity.
- 5 I understand that my involvement in the project will not affect my relationship with my pharmacist or doctor in their management of my health. I also understand that I am free to withdraw from the project at any stage and any of my data that has been collected. My withdrawal will not affect my legal rights, my medical care or my relationship with my pharmacist.
- 6 I understand that the trial will be conducted in accordance with the latest versions of the *National Statement on Ethical Conduct in Human Research 2007* and applicable privacy laws.
- 7 I understand that I am not giving up my legal rights by signing this consent form.
- 8 I understand that the project has received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee. I have been provided with adequate contact details if I wish to express any concerns of an ethical nature or complaints about the manner in which the project is conducted.

Name of Participant:.....

Address:.....

.....

Daytime telephone number: (03)..... What is your age?.....years

What is your gender? (circle) Male Female Are you a current smoker? (circle) Yes No

Signature of Participant:Date:.....

Please mail the signed consent form to the University of Tasmania by Friday 18th April in the postage paid envelope provided or fax it to 6226 7627. Consent form number: <patient ID>

Appendix 33. Patient information sheet



Understanding patient experiences with respiratory medication

PATIENT INFORMATION SHEET

We would like to invite you to participate in the following research project, conducted by the Tasmanian School of Pharmacy. You have been asked to participate because your community pharmacist noticed that you have received at least one supply of respiratory medication from the pharmacy over the past 12 months. We are interested in your participation regardless of whether you are still taking respiratory medication or not. We would like to assure you that your community pharmacist will not release any of your information to the Tasmanian School of Pharmacy without your consent.

We are interested in trying to learn more people's experiences with respiratory medication and to identify why people do or do not continue to take particular medications.

To help with this research, we will ask you some questions about your health and illness beliefs, and experiences with respiratory medication. We will also ask you a few questions regarding your age, gender and smoking status. These questions will be mailed to you in the form of a questionnaire. Your personal details will not be included in the questionnaire; therefore your responses will not be identifiable by the researchers. You may also be asked if you would like to take part in a face-to-face interview about your experiences with respiratory medication. To do the face-to-face interviews, we have teamed up with P Group Research, who are experts in this area, to ask you about how you use your medicines.

After completing and returning the questionnaire, you will receive a \$50 gift voucher, and if you are selected to also participate in a face-to-face interview, you will receive remuneration of \$70.

If you have any concerns or questions about the questionnaire or your participation in the study, please contact the University (contact details are on the following page). The results of this study may be published in the future, but your name will not be mentioned, and all of the information that you provide us with will be treated confidentially. You are free to not participate in the project if you wish. If this is the case, do not sign the consent form. If you agree to take part, please sign the attached consent form and return it to the University by Friday 18th April. Once you have signed the consent form, the Tasmanian School of Pharmacy will mail you the questionnaire and a reply paid envelope in which to return them. Then you may be contacted by P Group Research and asked if you would like to take part in a face-to-face interview. You are free to withdraw from participating in the study at any time if you wish.

The project has received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee. If you have any concerns of an ethical nature or complaints about the manner in which the project is conducted, you may contact the Executive Officer of the Tasmanian Human Research Ethics Committee (Tasmania) Network on 62267479 or human.ethics@utas.edu.au. You will need to quote ethics reference number H9842.

Results of this work may be published in pharmacy and medical journals and shown at pharmacy conferences. We can assure you that your personal details, the medications you take and other information we collect will not be given to anyone else. We will ensure all information about you will be kept private and confidential. All of the results are pooled together and then analysed.

Please do not hesitate to contact us if you have any questions or concerns regarding the project.

Yours sincerely



Bonnie Bereznicki B.Pharm (Hons)
Clinical Research Pharmacist and PhD Candidate
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 83 Hobart
Tasmania 7001
Telephone 6226 2191
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Bonnie.Bereznicki@utas.edu.au



Dr Shane Jackson B.Pharm (Hons) PhD MPS
Senior Research Fellow
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania



The research unit at the Tasmanian School of Pharmacy (UMORE; Unit for Medication Outcomes Research and Education) is a premier source of information, education and collaborative research in the assessment and improvement of medication outcomes.



P Group Research Pty Ltd specialised in delivering the highest quality in qualitative research and has available highly experienced consultants, all of which are AMSRS members and thus adhere stringently to the AMSRS Professional Code of Conduct and the Market and Social Research Privacy Principles. Their specialist interviewers have conducted hundreds of interviews with patients and are highly sensitive and empathetic to patient issues.

This study has received financial support from Boehringer Ingelheim

Appendix 34. Patient letter regarding questionnaire



Understanding patient experiences with respiratory medication

Dear <patient name>

Thank you for agreeing to participate in the project *Understanding patient experiences with respiratory medication*, being conducted by the Tasmanian School of Pharmacy and P Group Research. Your participation and support is vital to improve the management and quality of life of people for people with respiratory conditions and is thus greatly appreciated.

Please find enclosed a Patient Questionnaire for you to complete. Please be assured that all of your responses to the questionnaires will be anonymous. If have any queries or concerns about any part of the questionnaire, please don't hesitate to contact Bonnie Bereznicki at the Tasmanian School of Pharmacy, on the details below.

Once you have completed the questionnaire, please return it to the Tasmanian School of Pharmacy in the postage paid envelope provided.

We estimate that completion of the questionnaire will take 20-30 minutes of your time. Upon receipt of the completed questionnaire, the Tasmanian School of Pharmacy will send you a \$50 Coles Group and Myer Gift Card, which will be redeemable at Coles, Myer, Target, Kmart and Officeworks stores. All questionnaires are uniquely identified by a number, which will allow the researchers to mail you a Gift Card upon receipt of the completed questionnaire. The identification number will be removed from the questionnaire prior to data entry to ensure your responses are not identifiable.

Please also find enclosed a copy of your signed consent form for your own records.

Once again, we thank you for your assistance in our research.

Yours Sincerely,

A handwritten signature in black ink that reads 'Bereznicki'.

Bonnie Bereznicki B.Pharm (Hons)
Clinical Research Pharmacist and PhD Candidate
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 83 Hobart
Tasmania 7001
Telephone 6226 2191
Facsimile 6226 7627
Bonnie.Bereznicki@utas.edu.au

A handwritten signature in black ink that appears to read 'Shane Jackson'.

Dr Shane Jackson B.Pharm (Hons) PhD MPS
Senior Research Fellow
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania

This study has received financial support from Boehringer Ingelheim

Appendix 35. Patient questionnaire

Patient Questionnaire

Understanding patient experiences with respiratory medication

A research project being conducted by
the Tasmanian School of Pharmacy and P Group Research



Funded by Boehringer Ingelheim

Understanding patient experiences with respiratory medication

Patient Questionnaire Instructions

- The questionnaire contains a total of 21 questions.
- The questionnaire is made up of 2 parts:
 - Part A: Questions about your respiratory health
 - Part B: Questions about your health views, beliefs and feelings.
- Please answer **all** of the questions (unless otherwise instructed). Questions that may be left blank if they do not apply to you include **3b, 3c, 3d, 3e, 3f, 6, 8b** and **14**. All other questions require an answer to enable analysis. Questions 11-16 require a true/false answer. If the statement does not apply to you, please answer 'false' rather than leaving it blank.
- Please tick **one** box only for **each** statement as it applies to you.
- All of your responses will be anonymous.
- Once you have completed the questionnaire, please double-check that you have answered all of the questions as they apply and return the entire questionnaire to the Tasmanian School of Pharmacy in the reply paid envelope provided.
- All questionnaires are uniquely identified by a number, which will allow the researchers to mail you a \$50 Coles Group & Myer Gift Card upon receipt of the completed questionnaire. The identification number will be removed from the questionnaire prior to data entry to ensure your responses are not identifiable.
- If you have any queries or concerns about any part of the questionnaire, please contact Bonnie Bereznicki at the Tasmanian School of Pharmacy on the details below.
- Contact details for the Tasmanian School of Pharmacy:

Bonnie Bereznicki
Unit for Medication Outcomes Research and Education
Tasmanian School of Pharmacy
University of Tasmania
Private Bag 83 Hobart
Tasmania 7001
Telephone: 6226 2191
Facsimile: 6226 7627
Email: Bonnie.Bereznicki@utas.edu.au
- **Thank you for your participation!**

Part A: Questions about your respiratory health

1. Have **you ever worked for a year or more** in a job that regularly exposed you to dust, gas or chemical fumes? ☐ Yes ☐ No

2. Which **one** of the following best describes your home situation?

My home is
smoke free
☐

People occasionally
smoke in the house
☐

People frequently
smoke in the house
☐

3. a) Have you **ever** regularly smoked cigarettes? ☐ Yes ☐ No

If you answered YES, please answer the following five questions:
(If you have never regularly smoked cigarettes, go to question 4)

- b) Do you **now** smoke cigarettes (**as of one month ago**)? ☐ Yes ☐ No

- c) How old were you when you **first** started regular cigarette smoking?(age in years)

- d) **If you have stopped smoking cigarettes completely,** how old were you when you stopped?(age in years)

- e) **Over the entire time you smoked,** how many cigarettes did you smoke per day on average?(cigarettes per day)

- f) On average, **how many** cigarettes do you smoke per day **now**?(cigarettes per day)

4. Please indicate **how much respiratory trouble you have had in the past year**, by ticking one box in response to each of the following examples of chest trouble:

	Most days a week	Several days a week	A few days a week	Only with chest infections	Not at all
a) Over the last year , I have coughed:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Over the last year , I have brought up phlegm (sputum):	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Over the last year , I have had shortness of breath:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Over the last year , I have had attacks of wheezing:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. **During the last year**, how many severe or very bad attacks of respiratory trouble have you had?

More than 3 attacks	3 attacks	2 attacks	1 attack	No attacks
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

6. **During the last year**, how long did the worst attack of respiratory trouble last?
(If you had no severe attacks, go to question 7)

A week or more	3 or more days	1 or 2 days	Less than a day
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. **Over the last year**, in an average week, how many **good** days (with little or no respiratory trouble) have you had?

None	1 or 2	3 or 4	Nearly every day	Every day
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8. a) Do you have a wheeze? ☐ Yes ☐ No (If **no**, go to question 9)
b) If **yes**, is it worse in the morning? ☐ Yes ☐ No

9. How would you describe your respiratory condition?

The most important problem I have	Causes me quite a lot of problems	Causes me a few problems	Causes no problem
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. This is a question about how your respiratory trouble **affects your current work** (if you are currently employed) **or affected your previous work** (if you were previously employed)

If you have **ever** had paid employment:

My respiratory trouble made me stop work	My respiratory trouble interferes/interfered with my work or made me change my work	My respiratory trouble does/did not affect my work
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

11. This is a question about what activities **usually make you feel breathless**
(Please tick **one** box in response to **each** statement **as it applies to you recently**)

	True	False
a) Sitting or lying still usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>
b) Getting washed or dressed usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>
c) Walking around the home usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>
d) Walking outside on the level usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>
e) Walking up a flight of stairs usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>
f) Walking up hills usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>
g) Playing sports or games usually makes me feel breathless	<input type="checkbox"/>	<input type="checkbox"/>

12. Another question about your cough and breathlessness

(Please tick **one** box in response to **each** statement **as it applies to you recently**)

	True	False
a) My cough hurts	<input type="checkbox"/>	<input type="checkbox"/>
b) My cough makes me tired	<input type="checkbox"/>	<input type="checkbox"/>
c) I get breathless when I talk	<input type="checkbox"/>	<input type="checkbox"/>
d) I get breathless when I bend over	<input type="checkbox"/>	<input type="checkbox"/>
e) My cough or breathing disturbs my sleep	<input type="checkbox"/>	<input type="checkbox"/>
f) I get exhausted easily	<input type="checkbox"/>	<input type="checkbox"/>

13. This is a question about **other effects your respiratory trouble may have on you**

(Please tick **one** box in response to **each** statement **as it applies to you recently**)

	True	False
a) My cough is embarrassing in public	<input type="checkbox"/>	<input type="checkbox"/>
b) My respiratory trouble is a nuisance to my family, friends, or neighbours	<input type="checkbox"/>	<input type="checkbox"/>
c) I get afraid or panic when I cannot get my breath	<input type="checkbox"/>	<input type="checkbox"/>
d) I feel that I am not in control of my respiratory condition	<input type="checkbox"/>	<input type="checkbox"/>
e) I do not expect my respiratory condition to get any better	<input type="checkbox"/>	<input type="checkbox"/>
f) I have become frail or an invalid because of my respiratory trouble	<input type="checkbox"/>	<input type="checkbox"/>
g) Exercise is not safe for me	<input type="checkbox"/>	<input type="checkbox"/>
h) Everything seems too much of an effort	<input type="checkbox"/>	<input type="checkbox"/>

14. This is a question about your **respiratory medication**

(If you are **not** receiving medication for your respiratory trouble, go to question 15)

(Please tick **one** box in response to **each** statement **as it applies to you recently**)

	True	False
a) My medication does not help me very much	<input type="checkbox"/>	<input type="checkbox"/>
b) I get embarrassed using my medication in public	<input type="checkbox"/>	<input type="checkbox"/>
c) I have unpleasant side effects from my medication	<input type="checkbox"/>	<input type="checkbox"/>
d) My medication interferes with my life a lot	<input type="checkbox"/>	<input type="checkbox"/>

15. This is a question about how **activities may be affected by your breathing**

(Please tick **one** box in response to **each** statement **as it applies because of your breathing**)

	True	False
a) I take a long time to get washed or dressed	<input type="checkbox"/>	<input type="checkbox"/>
b) I cannot take a bath or shower, or I take a long time	<input type="checkbox"/>	<input type="checkbox"/>
c) I walk more slowly than other people, or I stop for rests	<input type="checkbox"/>	<input type="checkbox"/>
d) Jobs such as housework take a long time, or I have to stop for rests	<input type="checkbox"/>	<input type="checkbox"/>
e) If I walk up one flight of stairs, I have to go slowly or stop	<input type="checkbox"/>	<input type="checkbox"/>
f) If I hurry or walk fast, I have to stop or slow down	<input type="checkbox"/>	<input type="checkbox"/>
g) My breathing makes it difficult to do things such as walk up hills, carry things up stairs, light gardening, dance, play bowls or golf	<input type="checkbox"/>	<input type="checkbox"/>
h) My breathing makes it difficult to do things such as carry heavy loads, dig in the garden, jog or walk quickly, play tennis or swim	<input type="checkbox"/>	<input type="checkbox"/>
i) My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast or play competitive sports	<input type="checkbox"/>	<input type="checkbox"/>

16. We would like to know how your respiratory trouble **usually affects your daily life**
(Please tick **one** box in response to **each** statement **as it applies because of your respiratory trouble**)

	True	False
a) I cannot play sports or games	<input type="checkbox"/>	<input type="checkbox"/>
b) I cannot go out for entertainment or recreation	<input type="checkbox"/>	<input type="checkbox"/>
c) I cannot go out of the house to do the shopping	<input type="checkbox"/>	<input type="checkbox"/>
d) I cannot do housework	<input type="checkbox"/>	<input type="checkbox"/>
e) I cannot move far from my bed or chair	<input type="checkbox"/>	<input type="checkbox"/>

17. Tick **one** statement which you think **best** describes **how your respiratory trouble affects you:**

It does not stop me doing anything I would like to do	It stops me doing one or two things I would like to do	It stops me doing most of the things I would like to do	It stops me doing everything I would like to do
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Part B: Questions about your health views, beliefs and feelings

18. Please circle the number that best corresponds to **your views about your respiratory condition** (the condition for which you received respiratory medication in the last 12 months)

a) How much does your respiratory condition affect your life?

0	1	2	3	4	5	6	7	8	9	10
no affect at all										severely affects my life

b) How long do you think your respiratory condition will continue?

0	1	2	3	4	5	6	7	8	9	10
a very short time										forever

18. (Continued)

Please circle the number that best corresponds to **your views about your respiratory condition** (the condition for which you were prescribed respiratory medication in the last 12 months)

c) How much control do you feel you have over your respiratory condition?

0	1	2	3	4	5	6	7	8	9	10
absolutely										extreme
no control										amount
										of control

d) How much do you think your treatment can help your respiratory condition?

0	1	2	3	4	5	6	7	8	9	10
not										extremely
at all										helpful

e) How much do you experience symptoms from your respiratory condition?

0	1	2	3	4	5	6	7	8	9	10
no										many
symptoms										severe
at all										symptoms

f) How concerned are you about your respiratory condition?

0	1	2	3	4	5	6	7	8	9	10
not at all										extremely
concerned										concerned

g) How well do you feel you understand your respiratory condition?

0	1	2	3	4	5	6	7	8	9	10
don't										understand
understand										very clearly
at all										

h) How much does your respiratory condition affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)

0	1	2	3	4	5	6	7	8	9	10
not at all										extremely
affected										affected
emotionally										emotionally

19. We would like to ask you about your personal views about medicines in general. These are statements other people have made about medicines in general. Please indicate the extent to which you agree or disagree **each statement** by ticking the appropriate box.

	Strongly agree	Agree	Uncertain	Disagree	Strongly disagree
a) Doctors prescribe too many medicines	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) People who take medicines should stop their treatment for a while every now and again	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Most medicines are addictive	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Natural remedies are safer than medicines	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Medicines do more harm than good	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f) All medicines are poisons	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g) Doctors place too much trust on medicines	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h) If doctors had more time with patients they would prescribe fewer medicines	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

20. Many people find a way of using their medication that suits them. This may differ from the instructions on the label or from what their doctor had said. Here are some ways in which people have said they use their respiratory medications. For each statement, please tick the box that **best applies to you**.

	Never	Rarely	Sometimes	Often	Always
a) I get confused about my respiratory medications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) I have strict routines for using my regular respiratory medications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) I keep my respiratory medications close to where I need to use them	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Understanding patient experiences with respiratory medication

<ID>

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20. (Continued)

Many people find a way of using their medication that suits them. This may differ from the instructions on the label or from what their doctor had said. Here are some ways in which people have said they use their respiratory medications. For each statement, please tick the box that **best applies to you**.

	Never	Rarely	Sometimes	Often	Always
d) I ensure I have enough respiratory medications so that I don't run out	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) I push myself to follow the instructions of my doctors	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f) I make changes in the recommended management to suit my lifestyle	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g) I vary my recommended management based on how I am feeling	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h) I put up with my respiratory problems before taking any action	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

21. Please complete all questions by ticking the box that best describes how you have been feeling in the past week. Your immediate reaction to each item will probably be more accurate than a long thought-out response.

a) I feel tense or wound up

Most of the time	A lot of the time	From time to time	Not at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

b) I still enjoy the things I used to enjoy

Definitely as much	Not quite so much	Only a little	Hardly at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

c) I get a sort of frightened feeling as if something awful is about to happen

Very definitely and quite badly	Yes, but not too badly	A little, but it doesn't worry me	Not at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

21. (Continued)

Please complete **all** questions by ticking the box that best describes **how you have been feeling in the past week**. Your immediate reaction to each item will probably be more accurate than a long thought-out response.

d) I get a sort of frightened feeling as if something awful is about to happen

Very definitely and quite badly	Yes, but not too badly	A little, but it doesn't worry me	Not at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

e) I can laugh and see the funny side of things

As much as I always could	Not quite as much now	Definitely not as much now	Not at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

f) Worrying thoughts go through my mind

A great deal of the time	A lot of the time	From time to time but not too often	Only occasionally
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

g) I feel cheerful

Not at all	Not often	Sometimes	Most of the time
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

h) I can sit at ease and feel relaxed

Definitely	Usually	Not often	Not at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

i) I feel as if I am slowed down

Nearly all the time	Very often	Sometimes	Not at all
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

j) I get a sort of frightened feeling like butterflies in the stomach

Not at all	Occasionally	Quite often	Very often
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

k) I have lost interest in my appearance

Definitely	I don't take so much care as I should	I may not take as much care	I take just as much care
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

21. (Continued)

Please complete **all** questions by ticking the box that best describes **how you have been feeling in the past week**. Your immediate reaction to each item will probably be more accurate than a long thought-out response.

l) I feel restless as if I have to be on the move

Very much indeed

☐

Quite a lot

☐

Not very much

☐

Not at all

☐

m) I look forward with enjoyment to things

As much as
I ever did

☐

Rather less
than I used to

☐

Definitely less
than I used to

☐

Hardly
at all

☐

n) I get sudden feelings of panic

Very often indeed

☐

Quite often

☐

Not very often

☐

Not at all

☐

o) I can enjoy a good book or radio or TV program

Often

☐

Sometimes

☐

Not often

☐

Seldom

☐

----- END OF QUESTIONNAIRE -----

Thank you for completing this questionnaire.

Before you finish please check that you have answered all of the questions.

**Please return the completed questionnaire to Tasmanian School of Pharmacy
in the reply paid envelope provided.**

Appendix 36. Discussion guide for qualitative interviews



COPD patient research: discussion guide

1. Introduction

Briefly explain the following points:

- ◆ **Research objectives:** to understand what it is like to live with a respiratory condition such as COPD/emphysema/chronic bronchitis, particularly how patients manage their condition on a day-to-day basis.
- ◆ **Confidentiality** and anonymity, privacy.
- ◆ **Timing:** interview will take about 60 minutes.
- ◆ **Commissioning client:** can be revealed at the end of the interview.
- ◆ **Pre-interview survey:** collect and confirm that questionnaire completed as per instructions.

2. Patient profile

~5 minutes

Briefly review demographics contained in pre-interview survey (family situation, employment status, income source, smoking history, does anyone else in the house smoke etc)

Using the Data Sheet provided, collect the following patient information:

- ◆ Self-reported diagnosis (note that if the patient believes they have asthma or something other than COPD, refer to whichever 'respiratory condition' the patient believes they have throughout the remainder of the interview);
- ◆ Co-morbid conditions;
- ◆ Therapeutic regimen for co-morbid conditions – brand and indication;
- ◆ Approximate monthly spend on managing [INSERT respiratory condition].

3. Patient experience

Fully explore, using the therapeutic buying process as an organising framework [i.e. origination → diagnosis → treatment choice/practice → fulfilment → persistence]

Explain we are interested to hear the patient's story right from the beginning. Encourage them to cast their minds back and walk the interviewer through their total experience in as much detail as they can recall.

3.2 Origination: Explore how the patient came to be diagnosed with [INSERT respiratory condition] in the first place.

~5 minutes

Prompt as required:

- What led to you being prescribed medicine for a respiratory condition (e.g. did they just go the doctor/spontaneously? Prompted by family/friends? Prompted by healthcare professional?) Why/why not?
- What were their symptoms? Severity? Did they have a cough that wouldn't go away (and what time of year was it)?



- What were they told they had?
- How did they manage their condition prior to initial presentation?
- What did they think/feel about their symptoms at the time?

3.2 Diagnosis Explore patient's understanding of their diagnosis and prognosis, as well as associated beliefs, attitudes and feelings. *~5 minutes*

Establish/confirm approximate time (month and year) of diagnosis [cross reference with Recruitment Schedule]

Prompt as required:

- How did the doctor go about finding out what was wrong? What questions were asked? What tests were done? [NOTE: capture whether the initiating doctor was hospital based or a GP]
- What diagnosis did the doctor give? What were impressions of ease/difficulty for the doctor to arrive at a diagnosis?
- What explanation/information did the doctor provide? [If initiated in hospital, ask: Did your GP provide any more information or explain it differently]
- How did patient interpret/make sense of the diagnosis?
- What was previously known/understood/felt about the condition (e.g. familiar versus unfamiliar, inevitable with ageing, risk factors)? Extent of information seeking behaviour? Information sources?
- What was patient's understanding of the prognosis?
- Explore associated feelings/emotions with diagnosis/prognosis. [PROBE FULLY, LADDERING]

3.3 Treatment choice Explore patient's recall of treatment choice, as well as beliefs and attitudes towards treatment and relationship with doctors. *~10 minutes*

Explore patient's relationship with healthcare professional (specifically GP and respiratory physician), particularly duration, trust (confidence, faith), degree of perceived empathy and quality of communication. Also explore patient's relationship with their local pharmacist.

Prompt as required:

- What is nature of patient/healthcare professional relationship– describe typical consult [PROBE FULLY, LADDERING ON EMOTIONAL RESPONSES]
- How patient feels about their GP/respiratory physician
- How patient thinks their GP/respiratory physician feels about the patient i.e. reciprocated feelings (e.g. like or dislike? Warm or cold? Brusque or leisurely? Task-focussed/holistic approach? etc.)



Explore approach GP originally proposed to treating the diagnosed condition (e.g. referral to respiratory physician? Therapy initiation versus therapy review or modification? Multidisciplinary approach? Behaviour modification?)

Prompt as required:

- What was GP's approach to treatment/management (e.g. medication trial & error versus set and forget? Smoking cessation? Other lifestyle modification? Pulmonary rehabilitation? Holistic versus one-dimensional, i.e. medication only)
- What was the extent of patient involvement in choice of treatment regimen?
- What were their initial expectations of treatment (e.g. symptom relief, time frame, side effects, cost)
- What happened when first started on medication? (e.g. started to feel better? No change? Felt worse?) What was their response to this?
- Explore associated feelings/emotions associated with treatment (e.g. relief that doing something? Disappointment that open-ended? Onerous burden or top of all other medications? Impatience/frustration?)
[PROBE FULLY, LADDERING]

3.4 Day-to-day practice Explore how COPD is managed on a day-to-day basis currently - behaviours, habits, attitudes/feelings *20 minutes*

- Invite respondent to describe their usual approach, including medication, lifestyle, psychosocial, alternative/complementary therapies, activities of daily living and **carer arrangements**. [Probe on involvement of carer/partner, what do they think of all this? e.g. do they know a lot about it, do think it's a load of rubbish, do they nag the respondent into taking their medication?]
- Medication 'show and tell' Invite respondents to describe in as much detail as possible their medication regimen (i.e. what, when, how)

Encourage demonstration, observe for any physical barriers/impediments.

Complete sections A & B of Data Sheet, i.e. record current/past therapeutic regimen for COPD i.e. brand, indication, when initiated and current practice.

Prompt as required:

- Explore extent that respiratory medication regimen is routinely taken (Where administered? When? How?) Any exceptions? Differentiate between 'normal' and exacerbated states.
- Explore perceived role of respiratory medication within overall COPD management approach (e.g. central versus peripheral?)
- Establish mental model of how they think about their respiratory medication (e.g. management versus preventative versus rescue OR everyday/regular versus sometimes/occasional/seasonal – are they more likely to take their medication at certain times of the year?)



Explore how they think about adherence:

Probe: Some people are fairly casual about taking medication as instructed, whereas others follow instructions to the letter. Where do you fit on that continuum?

- Refer to selected survey items (adherence and health behaviours) and **probe fully** on underlying thinking behind ratings given.
- Probe for any other facilitators and barriers to adherence (probe on seasonality if this was an issue raised).

Ask Past SPIRIVA users:

Invite them to tell story of what happened that were initiated on SPIRIVA but not currently on it [**NB. take neutral non judgmental approach**]

- How long were you on SPIRIVA? (e.g. did not fill initial script at all versus came off after some time)
- How did it come about? (Whose decision? how was it made?)
- How successful was decision to come off? (Any regrets?)

3.5 Fulfilment Explore typical approach to getting scripts filled. **~5 minutes**

- What is usual approach to getting any type of script filled? (e.g. same day versus when convenient? same/different pharmacist? self/carer? phone/in person?)
- What drives preferences? (e.g. convenience, cost, relationship with pharmacist)
- What is usual approach when getting repeat respiratory medication scripts? (Wait until finished and then refill? refill before finished?) Why?
- What circumstances would make this change?
- What advice do you get from the pharmacist? Is there anything extra that the pharmacist could do for you, such as providing more information? (Probe on GP as well)

3.6 Persistence Explore motivations and behaviours regarding persistence with respiratory medication **~10 minutes**

- How is treatment success gauged? What measures/criteria are used to determine success. [Probe on: are they looking to relieve breathlessness/symptom relief or is it related to longer term goals like being able to spend quality time with family/on family activities]
- What are expectations/behaviours regarding timeframe for persistence

Prompt as required:

- How long do you usually give any medication to work/be effective?
- Is expectation/behaviour in relation to COPD any different to that for other chronic conditions?



- What arrangements are in place for ongoing monitoring by GP/respiratory physicians? Who drives it? How satisfactory? How could it be improved?

Ask Current SPIRIVA users:

- Establish how long been on SPIRIVA.
- Have you ever felt like stopping/changing medication? Why/ why not? (Probe on seasonality)
- If yes, what action have you taken (e.g. done nothing, raised it with GP, taken a treatment holiday)

Ask all:

- How do they see the future (progressive decline? As good as it gets? Potential to improve?) **Probe fully** on associated feelings.

3.3 Concluding comments

- Is there anything else they would like to raise or share in relation to living with COPD?
- Thank respondent, provide incentive and get them to sign incentive sheet.